United States Court of Appeals

for the Second Circuit



APPELLEE'S APPENDIX

74-1507

United States Court of Appeals

FOR THE SECOND CIRCUIT

Docket No. 74-1507

OTIS CLAY,

Plaintiff-Appellant,

—against—

DOCTOR WILLIAM R. MARTIN, DOCTOR PETER A. MANSKY, and DOCTOR DONALD R. JASINSKI,

—and—

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF PRISONS,

—and—

THE UNITED STATES,

Defendants-Appellees.

APPEAL FROM A JUDGMENT OF THE UNITED STATES DISTRICT COURT FOR THE SOUTHERN DISTRICT OF NEW YORK

DEFENDANTS-APPELLEES' APPENDIX

HON. PAUL J. CURRAN
United States Attorney
Southern District of New York
United States Courthouse
Foley Square
New York, New York 10007
Attorney for Defendants-Appellees

UNITED STATES COURT OF APPEALS
FILED
SEP 20 1974
CLERK

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List of Docket Entries

Date *Proceedings*

5/24/71—Filed complaint and issued 20 days summons.

5/24/71—Filed order granting the filing thereof without prepayment of fees. Sugarman, *Ch. J.*

6/16/71—Filed summons with Marshal's return

Served Dr. Jasinski. Unable to serve on 6/3/71.

Served Dr. Jasinski, personally on 6/9/71.

Served Dr. Mansky, by Dr. Martin on 6/9/71.

Served Mr. Carlson, Chief of Bureau of Prisons by certified mail to Bureau of Prisons, Washington, D. C.

Served the Surgeon General on 6/8/71 by certified mail to Surgeon General, Washington, D. C.

Served the Attorney General of the United States by certified mail to Attorney General, Washington, D. C.

Served the United States Attorney of the Southern District of New York on 6/8/71.

8/ 9/71—Filed answer of defendants Dr. Martin, Dr. Mansky, Dr. Jasinski, the Surgeon General, the Attorney General, The Bureau of Prisons and the United States.

10/27/71—Filed rebuttal to and memorandum and opposition of said Attorney, Whitney North Seymour, Jr., for the defendants.

8/14/73—Filed affidavit of Ronald Parker of service of interrogatories upon Whitney North Seymour, Jr., United States Attorney on 8/9/73.

8/14/73—Filed plaintiff's interrogatories.

List of Docket Entries

Date	*Proceedings*
9/14/73	Filed stipulation and order that the time for defendants to answer plaintiff's interrogatories is extended to 10/12/73. Ryan, *J.*
10/25/73	Filed defendants' answers and objections to interrogatories.
11/19/73	Pre-trial conference held.
11/20/73	Filed defendants' further answers to interrogatories.
11/26/73	Filed order dismissing action for lack of prosecution, without prejudice and without costs. Ryan, *J.*
12/ 6/73	Filed plaintiff's affirmation and notice of motion for relief from order of dismissal. Returnable 12/6/73.
12/ 7/73	Filed memo. Endorsed motion filed 12/6/73. Carl O. Callendar is to file a notice of appearance for plaintiff herein within five days from the date hereof. The order of dismissal is vacated and the action is restored. Complaint is stricken with leave to the plaintiff to file within 25 days from the date hereof, an amended complaint. Defendants to file an answer to said amended complaint within 20 days after it is served. In the event that the directions of paragraphs 1, 2 and 3 are not complied with, an order of dismissal may be submitted on 5 days notice of settlement. So Ordered—Ryan, *J.* Mailed notices.
12/14/73	Filed notice of appearance for attorney for plaintiff.
1/ 3/74	Filed amended complaint.

List of Docket Entries

Date	*Proceedings*
1/23/74	Filed answer to amended complaint.
1/25/74	Filed plaintiff's notice of demand for jury trial.
2/25/74	Filed defendants' notice of motion to dismiss complaint. Returnable 3/7/74.
2/25/74	Filed affidavit of William S. Brandt in opposition to plaintiff's motion and in support of a motion to dismiss.
2/25/74	Filed defendants' memorandum of law.
3/ 7/74	Filed plaintiff's affirmation.
3/14/74	Filed plaintiff's notice of motion re: amended complaint. Returnable 2/18/74.
3/14/74	Filed affirmation of Carl O. Callender.
3/14/74	Filed memo. Endorsed on motion dated 3/14/74. Plaintiff's motion to serve a further amended complaint is denied and defendants' motion to dismiss is granted. Clerk is directed to enter judgment promptly. Ryan, *J.* Mailed notice.
4/19/74	Filed memo. Endorsement on notice of appeal. Leave to appeal in forma pauperis is granted. Ryan, *J.* Mailed notice.
4/19/74	Filed plaintiffs' notice of appeal from the final judgment of 3/14/74. Mailed notice.
5/28/74	Certified record to the United States Court of Appeals.
5/28/74	Filed letter from Otis Clay to Judge Ryan.

A 4

MOTION FOR CIVIL ACTION (COMPLAINT)

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY
Petitioner

-v-

DOCTOR MARTIN)
DOCTOR MANSKY) U. S. Penitentiary
DOCTOR JENESKY) Lexington, Ky.

THE SURGEON GENERAL)
THE ATTORNEY GENERAL (
THE BUREAU OF PRISONS) Washington, D.C.
THE U. S. GOVERNMENT)

Respondents

Civil NO.

Re: MOTION FOR CIVIL ACTION

MOTION FOR CIVIL ACTION

Comes now Otis Clay, hereinafter refered to as the Petitioner, Petitioner without counsel, moves this Honorable Court, against the Respondents in a Civil Action to Show Cause, and so order the Respondents named herein from the U.S. Penitentiary, Lexington, Ky., and Washington, D.C., to show why the Petitioner has been subjected to inhumane treatment.

STATEMENT OF FACTS

I, Otis Clay, Petitioner, being duly sworn, deposes and says, that this is a true statement to the best of my knowledge. I was transfered from the U.S. Prison in Atlanta, Georgia, to the Addiction Research Center in Lexington, Kentucky, on or about July 27, 1968, and shortly after arriving there I was given a complete physical examination, and found to be in very good health, in fact, because of my good physical condition, I was chosen to participate in a number of different tests at this Research Center.

ONLY COPY AVAILABLE

I realize that these tests were on a voluntary basis, but never the less, I was assured that nothing would be injected into my body, that would do permanate harm. On or about the last part of May, 1970, I, Otis Clay and another inmate by the name of Mr. Howard was called to the Research Ward, to be instructed to undergo a special test.

I was given a pamphlet to read, which stated a short history of the drug that would be administered. This pamphlet clearly stated, that the drug, which is unknown to me, had never been tested on human beings, but had been tested on various animals. It also stated that this drug had caused bad heart affects on most of the animals, and when I read this part of the pamphlet, I challenged Doctor Martin's effort to unject me with this drug.

Doctor Martin and his associates assured me that there was absolutly nothing to fear, that they would never inject any drug into me that would be harmful, they further stated that the amount of the drug that would be injected into me would only be one hundreth of the amount that was injected into the animals. After this conversation with Doctor Martin and his associates, I did agree to be injected with this unknown drug. After being unjected the first time with this drug, I felt twice my fifty some odd years old, and after the second shot I was complety exhausted. I have gone through more than two years of other tests not similar to this one, I was not affected by these tests, other than this particular test given by Doctor Martin and his staff. Therefore, I state that Doctor Martin and his staff, did in fact inject this harmful drug into me causing a severe heart attack.

Point 1. For these reasons as follows-----I was given an E.K.G. electro cardiagram test before the drug was injected, and one hour after the drug injection, I was given a second E.K.G. test. Therefore, again I state, that this drug, does have an effect on my heart, causing this condition. Otherwise there would have been no need for the E.K.G. tests.

Point 2. Furthermore, I do state, that one week later, after Doctor Martin reassured me that nothing would happen to my heart. And after giving the E.K.G. test again, before and after the drug shot, I did in fact suffer from a severe heart attack. I summoned the guard on duty and complained about this severe chest pain. He said, "He had never seen me in this condition before", and he then called the aide in the Research Ward, and in return this aide called Doctor Martin. In return Doctor Martin instructed his aide to give me and E.K.G. test, and then he, Doctor Martin and his staff did arrive at the ward expecting that something would happen to my heart from this drug. When I was taken to the ward, Doctor Martin ordered another E.K.G. test, and while I was taking this test, Doctor Martin and his staff, did comment that I was suffering from a severe heart attack. They in return rushed me to the C.R.C., Correctional Research Center, where I remained there for about six weeks under observation. I still complained about the pain. I was told that it would soon go away. After this six week period, I was returned tothe A.R.C. Ward, where in fact I did not get any rest at all, due to the fact that there were six of seven other men there suffering withdrawal from their drug addiction.

Point 3. Four months after this heart attack,I put in a Writ of Habeas Corpus to be brought to New York. This Writ of Habeas Corpus was denied, and I was then sent to Atlanta, Georgia. I spent another two months in Atlanta, and then was sent to Levenworth, while there I wrote to the Honorable Judge Motely for relief in my case, and that brings us up to this date.

I, Otis Clay, herein known as the Petitioner state, I am a citizen and resident of the State of New York, and I was sentenced in New York, also I am here on a Writ of Habeas Corpus from Levenworth on this matter before the Honorable Judge Motley.

I, Otis Clay, herein known as the Petitioner am presently incarcerated at the Federal Detention Headquarters, at 427 West Street, New York, New York.

The Respondents in this Civil Action are as follows:

Doctor Martin
Doctor Mansky
Doctor Jenesky
} U. S. Penitentiary, Lexington, Ky.

The Surgeon General
The Attorney General
The Bureau of Prisons
The U. S. Government
} Washington, D.C.

I, Otis Clay, herein known as the Petitioner, hold Doctor Martin directly responsible for issuing the orders to his aide along with his staff for issuing the two shots of the harmful drug that caused this severe heart attack.

I also state that Doctor Martin and his staff did knowingly have the knowledge what effects this drug would have on my heart, as I stated earlier in my statement.

I go on and state, I hold the Suggeon General responsible for this act of Doctor Martin and his staff for allowing them to test unknown drug to be used on Federal Prisoners under his medical supervision.

Furthermore, I hold the Bureau of Prisons also responsible for allowing the practice of this Research Staff to use Federal Prisoners as Guinea Pigs, in Lexington, Kentucky.

I further state that the Attorney General does in fact know of these practices, and could in his power prevent such acts of inhuman nature, mostly performed on Black and Latin Federal Prisoners.

And furthermore, I also detest these acts on humans like myself, a man with a thirty (30) year history of drug addiction, and under the Law considered Mentally Incompentent. I state that the Honorable Court and Honorable Judges, the people of this Country should in fact be aware of these inhumane acts and tests that are being performed on Federal Prisoners like myself, before they sentence anymore human beings to a Prison again.

I claim the figure of Two Million Dollars ($2,000,000,000,00) as compensation.

I base my claim to this amount for the reasons set forth in this claim. I have suffered severe heart attacks since these tests, the health I was enjoying has been impaired. My earning power is now diminished.

I claim that the Government has used my body for these inhuman tests, and ask this Honorable Court for relief in this case, as I feel I have already paid my debt to soceity, in the recent tests I have undergone in these past two years, while a Federal Prisoner. I pray this Honorable Court grant me an early release, so that I may live my few remaining years with my family.

Wherefore; Petitioner humbly prays that this Honorable Court grant him leave to proceed with this Motion of his Civil Action.

Respectfully Submitted:

Otis Clay

OTIS CLAY - Petitioner

Sworn to and subscribed
before me this 12th day
of June, 1971.

"AUTHORIZED BY ACT OF JUNE 10th, 1935
TO ADMINISTER OATHS (28 U.S.C. 4004)".

A 9

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

----------X

OTIS CLAY
Petitioner

-v-

UNITED STATES OF AMERICA
Respondent

----------X

Application for leave to proceed in Forma Pauperis

Before me, the undersigned authority came Otis Clay, who after being duly sworn according to law, on oath deposes and says:

1. That he is a citizen of the United States and of legal age; and--

2. That because of his poverty, he is unable to pay the cost of the instant cause of action or to give security for the same; and--

3. That he is a pauper within the meaning of the law. (Adkins v. Dupont) 335 U.S. 331 and title 28 U.S.C. ss 1915, and--

4. That he seeks redress in good faith to obtain the relief to which he verily believes he is entitled.

Wherefore, it is respectfully requested that this Court grant leave to proceed herein in Forma Pauperis, for otherwise an injustice will be foreclosed relief by reason of his inability to pay the cost thereof.

Otis Clay
OTIS CLAY - Petitioner

Subscribed and sworn to before
me this 12th day of May 1971.

[illegible]

CERTIFICATE OF SERVICE

It is hereby Certified that a true copy of the attached Motion has been mailed to the United Sates Attorney this____day of_____, 19__, and original and one carbon copy to the Clerk of the United States District Court for filing as prescribed to by law.

Otis Clay
OTIS CLAY - Petitioner

Subscribed and sworn to before me this 12th day of May 1971.

[illegible] JULY 7, 1955
TO ADMINISTER OATHS (18 U.S.C. 4004)".

A 11

71 CIV. 2306

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY

Petitioner

-v-

DOCTOR MARTIN, DOCTOR MANSKY, DOCTOR JENESKY } U. S. Penitentiary Lexington, Ky.

THE SURGEON GENERAL, THE ATTORNEY GENERAL, THE BUREAU OF PRISONS, THE U.S. GOVERNMENT } Washington, D.C.

Respondents

Civil No._____

NOTICE OF MOTION

Please take notice that upon the Motion and Statement of facts of the Petitioner herein, Otis Clay, the instant cause of action will come on before this Honorable Court for a hearing on the Court's first Motion Date, or as soon thereafter as the calender permits.

Otis Clay

OTIS CLAY - Petitioner
427 West Street
New York, New York

ANSWER A 12

Filed 8/9/71

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY,

Plaintiff,

- v -

DR. MARTIN; DR. MANSKY; DR. JENESKY; U.S. Penitentiary, Lexington, Kentucky; THE SURGEON GENERAL; THE ATTORNEY GENERAL; THE BUREAU OF PRISONS; THE UNITED STATES GOVERNMENT, Washington, D.C.,

Defendants.

ANSWER

Pro Se 71 Civ. 2306

Defendants, DR. MARTIN, DR. MANSKY, DR. JENESKY, THE SURGEON GENERAL, THE ATTORNEY GENERAL, THE BUREAU OF PRISONS, and THE UNITED STATES GOVERNMENT, by their attorney, Whitney North Seymour, Jr., United States Attorney for the Southern District of New York, for their answer to the motion for civil action herein (the "Complaint"), respectfully allege:

1. They deny the allegations contained in the first paragraph of the Complaint and aver that this "MOTION FOR CIVIL ACTION" is a complaint filed pursuant to 28 U.S.C. §§ 2671-2680.

2. They deny the allegations contained in the second paragraph of the Complaint except to admit that on the basis of medical history, physical examination and laboratory testing plaintiff, Otis Clay ("Clay"), was found to

be in good health after his transfer from the United States Penitentiary in Atlanta, Georgia to the Addition Research Center in Lexington, Kentucky on or about July 24, 1968.

3. They admit each and every allegation contained in Point 3 and in the third, sixth, seventh and eighth paragraphs of the Complaint.

4. They deny the allegations contained in the fourth paragraph of the Complaint except admit that Clay was given a "pamphlet" and aver that such "pamphlet" was a consent form which Clay signed prior to receiving the injections of the drug EN-1639A.

5. They admit each and every allegation contained in sentences one and two of the fifth paragraph of the Complaint and deny each and every allegation contained in sentences three, four and five of such paragraphs.

6. They admit each and every allegation contained in sentence one of Point 1 and deny each and every allegation contained in sentences two and three of such Point.

7. They deny allegation in Point 2 except admit that Clay did sustain a myocardial infarct, the first symptoms of which appeared five days after Clay received his final injection of the drug EN-1639A.

8. They deny the allegations contained in the ninth paragraph of the Complaint except admit that Dr. Martin supervises the research to which reference is made in the Complaint.

9. They deny each and every allegation contained in the tenth, twelfth, thirteenth, fourteenth, fifteenth and seventeenth paragraphs of the Complaint.

10. They deny the allegations contained in the eleventh paragraph of the Complaint except admit that pursuant to 42 U.S.C. §241, the Surgeon General has general authority to conduct research of the kind involving Clay.

11. They deny the allegations contained in the sixteenth paragraph of the Complaint except admit that Clay did sustain a myocardial infarct, the first symptoms of which appeared five days after Clay received his final injection of the drug EN-1639A.

FIRST AFFIRMATIVE DEFENSE WITH RESPECT TO ALL DEFENDANTS.

12. This Court lacks subject matter jurisdiction over this action.

SECOND AFFIRMATIVE DEFENSE WITH RESPECT TO ALL DEFENDANTS.

13. The Complaint fails to state a claim upon which relief can be granted with respect to any of the defendants herein.

WHEREFORE, the Defendants, Dr. Martin, Dr. Mansky, Dr. Jenesky, The Surgeon General, The Attorney General, The Bureau of Prisons, and The United States Government demand judgment in their favor and against plaintiff Otis Clay,

H:jeb
-1654

dismissing the Complaint with prejudice.

Dated: New York, New York

August 9 , 1971.

WHITNEY NORTH SEYMOUR, JR.
United States Attorney for the
Southern District of New York
Attorney for Defendants
Dr. Martin, Dr. Hinsky,
Dr. Janesky, The Surgeon General,
The Attorney General,
The Bureau of Prisons,
The United States Government

By: _____
DENNIS J. HELMS
Assistant United States Attorney

Office and Post Office Address:
United States Court House
Foley Square
New York, New York 10007
Telephone: (212) 264-[illegible]

REBUTTAL TO AND FOR MEMORANDUM AND OPPOSITION OF SAID ATTORNEY, WHITNEY NORTH SEYMOUR, Jr., FOR THE DEFENDANTS

UNITED STATES DISTRICT [illegible]
IN AND FOR
SOUTHERN DISTRICT OF NEW [illegible]

OTIS CLAY, Pro Se,

Plaintiff,

vs.

DR. MARTIN, DR. MANSKY, DR. JELESKY, U.S. PENITENTIARY, LEXINGTON, KENTUCKY;

THE SURGEON GENERAL, THE ATTORNEY GENERAL, THE BUREAU OF PRISONS, THE UNITED STATES GOVERNMENT, et al, WASHINGTON, D.C.,

Respondents.

CIVIL ACTION NO. 71 Civ. 2306

REBUTTAL TO AND FOR MEMORANDUM AND OPPOSITION OF SAID ATTORNEY, WHITNEY NORTH SEYMOUR, Jr., FOR THE DEFENDANTS

Comes now, Otis Clay, hereafter known as petitioner in the above entitled action, who moves and motions this Honorable Court by averment in support of law and fact that, after being duly sworn, says and deposes:

(1) That petitioner cannot find or obtain the relief sought under the provisions ascertained by Defendant's attorney, Whitney North Seymour, Esq., in Point 1 of said Answer to 71 Civ. 2306, which leaves an absences of fundamental fairness, which can be obtained under 28 U.S.C.A. 1346(b) whereas Tort Claims Procedure under 28 U.S.C.A. Sections 2671 and 2680 prohibits the available necessities to compensate, mainly relying upon the inexcusable factors which did cause injury and curtailed the life-span of the petitioner.

2. That petitioner respectfully submits argument as to the validity Whitney North Seymour, Esq. on the premises for the defendants when he, Atty. Seymour, projected in his averment,

"that this 'Motion for Civil Action' is a complaint filed pursuant to 28 U.S.C.A. §§2671 - 2680, deliberately, with knowing use, recognized the fault of the defendants and attempted to mislead the Court and evade the delicate question in the issue, which now tends to bring "civil Action for Deprivation of Rights"o T. 42 U.S.C., Sections 1983 - Subchapter I, Part III Enforcement Sec. 301 and 302, in and by leaving the door open to the events of corrective processing to a lay-mind of petitioner in propelling - Ch. 171 Tort Claims Procedure T. 28 U.S.C.A., Section 2680.

Exceptions - (a) Any claim based upon an actor omission of any employee of the government exercising due care, in the execution of a statute or regulation, whether or not such statute or regulation be valid, or based upon the exercise or performance or the failure to exercise or perform a discretionary function or duty on the part of a federal agency or an employee of the Government, whether or not the discretion involved be abused.

3. On the basis of denial of Point 2 "except to admit that on the basis of medical history, physical examination and laboratory testing plaintiff, Otis Clay ("Clay") was found to be in good health after his transfer from U.S. Penitentiary in Atlanta, Georgia to Addiction Research Center in Lexington, Kentucky on or about July 24, 1968. "Let the records speak for themselves 'subpoena duces tecum' which shall prove the entire allegation to be true.

4. That from the trier thereof, First Affirmative Defense With Respect to All Defendants.

12. "This Court lacks subject matter jurisdiction over this action,"

raises constitutional question as to 42 U.S.C. Section 1985 -

Conspiracy to Interfere With Rights - Sec. 1) Whereas Title 42 U.S.C. Subchapter II, Section 2000(a)(b) - Jurisdiction states:

Jurisdiction (a)

> "The district courts of the United States shall have jurisdiction of proceedings instituted pursuant to this subchapter and shall exercise the same without regard to whether the aggrieved party shall have exhausted any administrative or other remedies that be provided by law."

Also see: Title 28 U.S.C.A, Section 1331(a).

That on the basis that petitioner is a lifelong resident of New York, having family and security and a taxpayer, avers with support herein under 28 U.S.C.A., Section 1401(a)(1) and (b) constitute every right to be heard in this jurisdiction.

3. That petitioner being a layman in the arts and science of law contends, "Defense Counselor Whitney North Seymour in his able and learned brief argues that the plaintiff should not be accorded a remedy for the actual injury or the mental anguish which has been imposed"; that for the reason that a plaintiff is given no remedy is abundantly clear when he is [illegible] in his efforts to secure a judgment upon a valid claim by a fictitious defense maliciously interposed.

From: Lee vs. Southern Home Sites Corp., 429 F. 2d 290, we can clearly see the essences, as this Honorable Court sees, of same to,

> "Purpose of damages is to place plaintiff in same position, so far as money can do it, as he would have been had there been no injury or breach of duty, that is, to compensate him for injury actually sustained."

The above is in answer to:

Second Affirmative Defense With Respect to All Defendants.

> 11. The complaint fails to state a claim upon which relief can be granted with respect to any of the defendants herein."

CONCLUSION

Wherefore, plaintiff moves that this Honorable Court conceive the "delicate questions" and order a hearing.

The Delicate Questions

1. Purpose of damages?

2. To compensate for?

3. Injury actually sustained?

In referring to these questions as delicate questions it means that close distinctions must be drawn to allow for even slight differances in the facts, and that it is difficult to lay down any hard and fast general rule which can be made to apply to any considerable number of cases, and in light of the instant matter and subject, a careful reading of the authorities cited by counsel for the defense of the case at bar will disclose the force of this statement. No two cases cited are similar as to the facts, and where liability has been sustained in one case and denied in the other, the opinions disclose the fact that the diverse results are not due to any great divergence in the views of the Court, but rather to nice distinctions as to differences in the facts. In other words, each case must stand upon its own merits as disclosed by the evidence, and the evidence in the case at bar has been revealed with the complete knowledge of defendants and defense attorney Whitney North Seymour at Point 7 of Defendant's answer in 1-Civ. 2006 - whereas subject only to broad general rules as to what constitutes negligence and the degree of care required. The question as to the general class into which any given case will fall is "the delicate question", and that question must be determined from the facts.

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IT WAS - IT DID OCCUR AND the injury actually sustained [illegible] cause hospitalization, placing plaintiff in the intensive care unit which has impaired, permanent damages. Plaintiff seeks compensation for damages.

Respectfully submitted,

Otis Clay

Otis Clay

28 U.S.C. §1331(a)

Jacobs v. U.S. 290 U.S. 13-1933 A suit for damage caused by flooding the Supreme Court said of the right to compensation.

That right was guaranteed by the Constitution. The form of remedy did not qualify the right. It rested upon the Fifth Amendment. Statutory recognition was not necessary. A promise to pay was not necessary. Such a promise was implied because of the duty to pay imposed by the Amendment. The suits were thus founded upon the Constitution of the U.S. 290 U.S. at 16.

See also: Hopkins v. Clemson Agricultural College, 222 U.S. 636, 646, 648-49 - 1911.

U.S. v. Lee, 106 U.S. 196 - 1882.

See, e.g. Agnello v. U.S., 269 U.S. 20 1925

Bell v. Hood, 327 U.S. 678 - 1946

Ex parte Young, 209 U.S. 123 - 1908.

An injunction 209 U.S. at 149. The questions that arises is whether there is a remedy that the parties interested may resort to by going into a federal court of equity, in a case involving a violation of a federal Constitution and obtaining a judicial investigation of the problem, and - an injunction. 269 U.S. at 149.

See also: e.g. Philadelphia v. Stimson, 223 U.S. 605 - 1912.

City of Mitchell v. Dakota Central Tel. Co., 246 U.S. 396, 407-08 - 1918.

Contral Kentucky Natural Gas Co. v. Railroad Comm'n, 290 U.S. 264 - 269-72 - 1933

Georgia Railroad and Banking Co. v. Red Wine, 342 U.S. 299, 1952.

See: Hill, Constitutional Remedies, 69 Colum L. Rev. 1109 - 1128 - 31 1969.

Chisholm v. Taylor, 114 U.S. 309, 309-10, 1884

[illegible] supra, at 1128.

[illegible] of Entick v. Carrington, 19 How.

St. Tri. 1029 1776.

INTERROGATORIES

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY,	:	
Plaintiff,	:	
-against-	:	
DOCTOR MARTIN; DOCTOR MANSKY and DOCTOR JENESKY of United States Penitentiary, Lexington, Kentucky,	:	CIVIL ACTION NO. 2306/71
and	:	INTERROGATORIES
THE UNITED STATES SURGEON GENERAL; THE UNITED STATES ATTORNEY GENERAL; THE DIRECTOR OF THE BUREAU OF PRISONS and the UNITED STATES GOVERNMENT all of Washington, D.C.	:	
Defendants.	:	

TO:
WHITNEY NORTH SEYMOUR, JR.
UNITED STATES ATTORNEY FOR THE
SOUTHERN DISTRICT OF NEW YORK or
DENNIS J. HELMS, ASSISTANT UNITED STATES ATTORNEY
ATTORNEYS FOR THE DEFENDANTS
FOLEY SQUARE
NEW YORK, NEW YORK 10007

The plaintiff request that the defendants in person, or by their agent or agents, answer under oath, in accordance with Rule 33 of the Federal Rules of Civil Procedure, the following Interrogatories:

1. State whether the drug EN-1639A is currently being administed to federal prisoners as part of drug testing programs or otherwise.

2. If the answer to Interrogatory No. 1 is in the negative state when the use of the drug EN-1639A was discontinued in federal prisons and state the reasons for such discontinuance.

3. State the number of federal prisoners to whom the drug EN-1639A was administered prior to the date that it was first administered to Otis Clay.

4. State to your knowledge the number of persons, other than federal prisoners listed in response to Interrogatory No. 3, to whom the drug EN-1639A was administered prior to the first date that it was administered to Otis Clay.

5. State the effects of the drug EN-1639A on the persons described in Interrogatories Nos. 3 and 4, including, without limitation, any injurious effects on the health of such persons.

6. List all research reports, studies, study plans, findings, and other written materials, relating to the drug En-1639A and known to you, whether published or unpublished and whether prepared for the United States Government or for any other persons or organizations.

7. State the number of federal prisoners to whom the drug EN-1639A was administered subsequent to the date it was first administered to Otis Clay.

8. State the number of persons, other than federal prisoners listed in response to Interrogatory No. 7, to whom the drug En-1639A was administered subsequent to the first date that it was administered to Otis Clay.

9. State the effects of the drug EN-1639A on those persons described in Interrogatories Nos. 7 and 8, including, without limitation, any injurious effects on the health of such persons.

10. Describe the federal prisoners to whom the drug EN-1639A has been administered at any time, including, without limitation, the ages, physical condition and prior history of drug use of such persons.

11. State to your knowledge whether any person to whom

the drug EN-1639A has been administered, in a federal prison or elsewhere, has complained of the effects of the drug EN-1639A and describe the nature of such complaints.

12. State whether any cardiovascular disorder was revealed by the medical examination of Otis Clan made by personnel of the federal prison at Lexington, Kentucky immediately prior to the initial administration of the drug EN-1639A to him.

Please take notice that a copy of such answers must be served upon the undersigned within 30 days after service of these Interrogatories.

Dated: August 3rd, 1973

CARL O. CALLENDER, ESQ.
COMMUNITY LAW OFFICES
176 East 106th Street
New York, New York 10029
(212) 369-2007

STIPULATION EXTENDING TIME TO ANSWER INTERROGATORIES

A 26

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

U.S. DISTRICT COURT
FILED 9-14-73
S.D. of NEW YORK

Otis Clay

Plaintiff

-v-

United States Surgeon General etal.

Defendants

Stipulation

71 Civ 2306 SJR

deny 9/13/73
answer due date interrogatories
Oct 12-1973
ptroia

IT IS HEREBY STIPULATED AND AGREED by and between the attorneys for the respective parties, that the time of the defendants within which to answer or object with respect to plaintiffs interrogatories dated August 3, 1973, is hereby extended from September 7, 1973, to and including the 12th day of October, 1973.

DATED: NEW YORK, NEW YORK
September 10, 1973

Carl O. Callender
Attorney for Plaintiff

SO ORDERED: 9-13-73

/s/ Sylvester J. Ryan
U.S.D.J.

Paul J. Curran
United States Attorney
Southern District of New York
Attorney for Defendant

TO: Carl O. Callender, Esq.,
Community Law Office
176 East 106th Street
New York, NY 10029

ANSWERS AND OBJECTIONS TO INTERROGATORIES

A 27

Filed 10/26/73

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY,

Plaintiff,

-v-

DR. MARTIN, et al., and
THE UNITED STATES GOVERNMENT,
Washington, D. C.,

Defendants.

ANSWERS AND OBJECTIONS TO INTERROGATORIES

71 Civ. 2306 STR

Defendants, by their attorney, Paul J. Curran, United States Attorney for the Southern District of New York, hereby answer or object to plaintiff's Interrogatories, dated August 3, 1973:

1. Yes.

2. Not applicable.

3. Plaintiff was one of the two federal prisoners who first received drug EN-1639A. Plaintiff received two doses. Four other patients received drug EN-1639A in the interim between plaintiff's first and second doses.

4. None.

5. The effects of drug EN-1639A are described in a published article, "Naltrexone, an Antagonist for the Treatment of Heroin Dependence -- Effects in Man", Archives of General Psychiatry, Vol. 28, June 1973, pp. 784-791, a copy of which is being provided to plaintiff herewith.

6. To the extent the information requested by this interrogatory is available to defendants and not privileged, it will be provided to plaintiff as soon as the undersigned has obtained it. Efforts to obtain it are presently in progress.

7. At least 29.

8. At least 37.

9. See answer to interrogatory 5.

10. Defendants restrict their response to this interrogatory to the program in which plaintiff was involved. All persons involved in that program were in good physical condition, ranged in age from 27 to 53, and had extensive histories of narcotic use.

11. See answer to interrogatory 5.

12. No.

Dated: New York, New York
October 26, 1973

Yours, etc.,

PAUL J. CURRAN
United States Attorney for the
Southern District of New York
Attorney for Defendants

By: HOWARD S. SUSSMAN

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A 29

Naltrexone, an Antagonist for the Treatment of Heroin Dependence

Effects in Man

William R. Martin, MD; Donald R. Jasinski, MD; Peter A. Mansky, MD, Lexington, Ky

Naltrexone (EN-1639A) is approximately 17 times more potent than nalorphine as an antagonist in man. It is virtually devoid of agonistic activity, including the ability to induce nalorphine-like dysphoric effects. Its duration of action is longer than that of naloxone, but shorter than that of cyclazocine. It is effective orally. When administered in a dose level of 50 mg/day, it produces a degree of blockade of the effects of morphine and heroin that is comparable to that obtained with 4 mg of cyclazocine per day orally. Naltrexone, thus, appears to be a relatively pure potent narcotic antagonist which is effective orally and which may have utility in the treatment of heroin and narcotic dependence.

While studying the narcotic antagonist cyclazocine, it was found that tolerance developed to its agonistic activity but not to its antagonistic activity. It was further observed that cyclazocine was orally effective and had a long duration of action. These findings suggested that it would be possible to maintain former narcotic dependent subjects on a dose of an antagonist that would prevent narcotics from exerting their euphorogenic and dependence-producing effects, and thus provide a circumstance where both physiological and conditioned behavior related to drug acquisition and to relapse could be extinguished.[1-3] Early clinical studies of Jaffe and Brill[3] and Freedman et al[4] indicated that select patients might indeed be helped by narcotic antagonists; however, the unpleasant agonistic effects of cyclazocine made stabilization on blocking doses difficult, and the fact that an effective blockade could be maintained for only 24 hours with a daily oral dose was not only an inconvenience for the patient but allowed the effects of narcotics to become manifest by omitting a single dose. In an extensive series of studies in man, the narcotic antagonist naloxone was found to be virtually devoid of agonistic activity[5]; however, it had a relatively short duration of action. Zaks et al[6] have been able, using very large doses of naloxone orally, to attain effective blockade of morphine for nearly 24 hours. It has been the consensus of opinion of investigators that for a narcotic antagonist to be optimally effective in the ambulatory treatment of narcotic addicts it must be administered in such a way that its effect would have an appreciable duration of action (one week to one month), that it should be devoid of agonistic activity, and that it should be a highly potent compound to permit its administration in a depot form.

Cyclazocine, which has an N-methylcyclopropyl substitution on the nitrogen, exhibited an exceedingly long duration of action in man.[7] On the assumption that its long duration of action was related to the substitution on nitrogen, we felt that it would be worthwhile to study the N-cyclopropylmethyl congener of naloxone. Information concerning the synthesis of this compound, naltrexone (EN-1639A), is available from the patent literature.[8] Blumberg et al[9-11] characterized some of the pharmacological properties of naltrexone and conducted toxicological studies in animals. Their findings indicated that naltrexone was nearly twice as potent as naloxone as an antagonist, that it had only slightly agonistic activity (eg, analgesia), and that it had a longer duration of action than naloxone.

This communication will summarize our findings with this compound in man.

Methods

These studies were conducted in prisoner postaddicts who volunteered for and gave informed consent to all phases of the studies. Prior to participating, all patients had a recent history and physical examination and the following laboratory work-up: Chest roentgenogram, electrocardiogram, blood tests (red, white, and complete blood cell counts, differential), sedimentation rate, hemoglobin value and hematocrit reading, urinalysis (specific gravity, pH, sugar, albumin values and microscopic), serology, and serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase levels. No patient had signs or a history of psychotic behavior.

In the initial phase 1 studies, 13 patients participated and re-

Accepted for publication Nov 30, 1972.

From the National Institute of Mental Health, Addiction Research Center, Lexington, Ky. Dr. Mansky is now with Lindeman Mental Health Center, Boston.

Reprint requests to NIMH Addiction Research Center, PO Box 2000, Lexington, KY 40507 (Dr. Martin).

ceived naltrexone in doses ranging from 0.01 to 80 mg subcutaneously and 0.5 to 100 mg orally. In these studies, blood pressure, pulse rate, respiratory rate, and pupillary diameter determined photographically were measured before and ½, 1, 2, 3, 4, 5 and 12 hours after the administration of naltrexone. An EKG was taken prior to and two hours after the drug administration. Patients and observers completed the single-dose questionnaire[12] at each observation period.

To further determine if naltrexone had agonistic actions, five patients received, orally, 30 mg of naltrexone in a cherry vehicle or the cherry vehicle alone on alternate weeks. Observations were the same as in the preceding study, except that the patients also completed the subjective effect questionnaire.[13] The differences between the pretreatment and treatment observations for the first five hours were summed. The differences between these sums for the naltrexone and vehicle treatment conditions were determined and their significance assessed during a *t* test.

The potency of naltrexone relative to nalorphine was assessed in five patients by its ability to precipitate abstinence in subjects dependent on 15 mg of morphine sulfate administered four times daily. This method has been previously described.[7] Briefly, a crossover design was employed in which patients received either 0.07 or 0.14 mg/70 kg of naltrexone or 1.5 or 3.0 mg/70 kg of nalorphine hydrochloride at weekly intervals and the intensity of abstinence was assessed. The relative potency and its 95% confidence limits were calculated.[14]

A comparison of the duration of action of naltrexone with naloxone, both administered subcutaneously, was made in nine subjects. Pupillary diameter was measured photographically at 0700 and 0730 in 3.5 foot-candles of light, and 25 mg of morphine sulfate were administered subcutaneously at 0800. Naloxone (1 mg) or naltrexone (0.5 mg) was administered together with the morphine or 3, 6, and 12 hours before the morphine. As a placebo control, saline was administered five hours before morphine. Patients received one of these nine treatment conditions at weekly intervals. The order of the treatments was randomized, and each patient received all treatment conditions according to a latin-square design. Following the administration of morphine, pupillary diameter was again determined at 0900, 1000, 1100, 1200, 1300, and 2000. At these times, patients and observers completed the single-dose opiate questionnaire[12] and patients completed a subjective effect questionnaire.[13] All medications were administered subcutaneously in a 0.5-ml volume under double-blind conditions.

To assess the duration of action of orally administered naltrexone, a cherry vehicle was administered orally at 0800, 1400, 2000, and 0200 at weekly intervals over a five-week period to five subjects. At 0800 patients received 30 mg of morphine. For four weeks the patients received 15 mg of naltrexone in one of each of the four cherry vehicles. On the fifth week none of the four vehicles contained naltrexone. On the sixth week the subjects received 15 mg instead of 30 mg of morphine and no naltrexone was administered. Doses of naltrexone were randomized and a latin-square design employed. Observations were the same as in the previously described studies.

The efficacy of chronically and orally administered naltrexone in antagonizing the effects of single doses of morphine and preventing the development of physical dependence to chronically administered morphine was assessed in nine subjects. In six subjects naltrexone was administered orally at 0600 and 1800 in a dose level of 15 mg twice daily. In one additional subject, the dose level was 25 mg twice daily. In two subjects, naltrexone was administered orally once daily in a dose level of 50 mg at 1200. During the control period, a cherry vehicle was administered and the effects of 15 and 30 mg of morphine on pupils and subjective state were assessed. Naltrexone in cherry syrup was substituted for the vehicle and patients were brought to their maintenance dose within several days. When patients had achieved their maintenance dose levels, two or more test doses of morphine were administered subcutaneously at 0800 and their effects on pupillary diameter and subjective state were assessed as described in the preceding study. Patients were then given morphine four times daily in increasing dose levels until a stabilization dose of 240 mg/day was attained. They attained their stabilization dose by the sixth day, were maintained on this dose level for 11 days and then abruptly withdrawn from morphine while continuing to receive naltrexone. Ten days after withdrawal from morphine, naltrexone was discontinued by the substitution of the cherry vehicle. The intensity of the abstinence syndrome was assessed using the method of Himmelsbach.[15] During this phase of the study, routine observations of vital signs as well as signs of abstinence were made three times daily, and patients and observers completed chronic-dose questionnaires (Figs 1 and 2) daily. Responses to question 5 have not been analyzed and sign and symptom scale scores have not been developed; thus, these data will not be reported.

Results

Dose Ranging of Naltrexone.—Most of the 11 subjects who received naltrexone subcutaneously (0.01 to 80 mg) identified it as a "blank" and reported that it produced either no subjective changes or relaxation, which is a common response following the administration of a placebo. A few subjects reported that they stretched or yawned following its administration. One subject had symptoms and signs such as scratching, talkativeness, and "coasting" following 2 and 25 mg of naltrexone, and both observers and the subject thought that an opiate had been administered. Another patient who received 70 mg of naltrexone became nauseated and irritable, had racing thoughts, and saw Disney-like characters when his eyes were closed. He slept well the night after he had received the drug; however, the following night he had a panic reaction which was related to a chest pain. Findings of a physical examination and EKG were normal at this time except for an increase in respiratory rate and some tremulousness. The panic reaction subsided after the administration of 100 mg of pentobarbital sodium intramuscularly. Another 50-year-old patient who had received, at weekly intervals, 0.1 and 0.2 mg doses of naltrexone suffered a coronary 5½ days after receiving his last dose. Most patients who received naltrexone orally reported no change; however, two patients became sleepy and identified naltrexone as a barbiturate. No EKG changes were seen following naltrexone administration. There was a trend for blood pressure to be elevated and pupils to be constricted.

To further determine whether naltrexone had agonistic activity, 30 mg/70 kg was compared with the cherry vehicle. The results of this experiment are summarized in Table 1. As can be seen, naltrexone significantly increased diastolic blood pressure and decreased body temperature. Pupils were slightly constricted. Subjective changes that were reported were not different from those reported under the placebo condition.

Relative Antagonistic Activity.—Naltrexone is approximately 17 times more potent than nalorphine in precipitating abstinence in patients dependent on 60 mg of morphine a day (Fig 3).

Duration of Action.—Figure 4 compares the duration of action of subcutaneously administered naltrexone (0.5 mg) And naloxone (1.0 mg) in blocking the effects of 25 mg of

A 31

Date_____

Name_____ No._____ Drug_____ Study _____

ANSWER ALL QUESTIONS ACCORDING TO HOW THIS DRUG IS AFFECTING PATIENT TODAY.

1. Has the patient shown a drug effect today? Yes_____ No_____

2. Does its effect resemble any of the following drugs? Check one or more.
   a. Dope (heroin) _____
   b. Barbiturate (goofball) _____
   c. Cocaine _____
   d. Amphetamines (speed, benny, Methedrine) _____
   e. Marihuana (pot) _____
   f. LSD _____
   g. Thorazine _____
   h. Miltown and Librium _____

3. Does the patient like its effects? (Check one)
   a. Dislike _____
   b. Don't care one way or the other _____
   c. Slightly _____
   d. Moderately _____
   e. A lot _____

4. Is the patient hooked? Yes_____ No_____

5. Have you observed any of the following signs in the patient today?
   a. Relaxed _____
   b. Tired _____
   c. Anxious _____
   d. Nervous _____
   e. Drunk _____
   f. Depressed _____
   g. Disheveled _____
   h. Unfriendly _____
   i. Primping _____
   j. Vomiting _____
   k. Soapboxing or rapping _____
   l. Stays to himself _____
   m. Driving _____
   n. Coasting _____
   o. Nodding _____
   p. Sleepy _____
   q. Scratching _____
   r. Uncooperative _____
   s. Rides the bed _____
   t. Complaining _____
   u. Can't sleep _____
   v. Irritable _____
   w. Moody _____
   x. Stays close to ward _____
   y. Room disorderly _____

6. Is the patient kicking? Yes_____ No_____

7. How do you think the patient feels?
   a. Very good _____
   b. Good _____
   c. Average _____
   d. Slightly bad _____
   e. Moderately bad _____
   f. Bad _____
   g. Very bad _____

Fig 1.—Chronic dosage attitude questionnaire (aide's rating)

A 32

Date_____

Name_____ No._____ Drug_____ Study _____

ANSWER ALL QUESTIONS ACCORDING TO HOW THIS DRUG IS AFFECTING YOU TODAY.

1. Have you felt a drug effect during the last 24 hours? Yes_____ No_____

2. Does its effects resemble any of the following drugs? Check one or more

a. Dope (heroin)		e. Marihuana (pot)	
b. Barbiturate (goofball) or alcohol		f. LSD	
c. Cocaine		g. Thorazine	
d. Amphetamines (speed, benny, Methedrine)		h. Miltown and Librium	

3. Do you like the effects? Check one

a. Dislike	
b. Don't care one way or the other	
c. Slightly	
d. Moderately	
e. A lot	

4. Are you hooked? Yes_____ No_____

5. Have you had any of the following feelings or symptoms or symptoms during the last 24 hours? Check the ones you have had.

a. Relaxed		m. Driving	
b. Tired		n. Coasting	
c. Anxious		o. Nodding	
d. Nervous		p. Sleepy	
e. Drunk		q. Skin itchy	
f. Pins and needles		r. Stomach cramps	
g. Rush or flush		s. Diarrhea	
h. Cold or chills		t. Gooseflesh	
i. Joint, bone, muscle or back pains		u. Can't sleep	
		v. Irritable	
j. Soapboxing or rapping		w. Weak	
k. Nausea or vomiting		x. Nervous or jumping stomach	
l. Feel hot			

6. Are you kicking? Yes_____ No_____

7. How do you feel?

a. Very good		e. Moderately bad	
b. Good		f. Bad	
c. Average		g. Very bad	
d. Slightly bad			

Fig 2.—Chronic dosage attitude questionnaire (patient's rating).

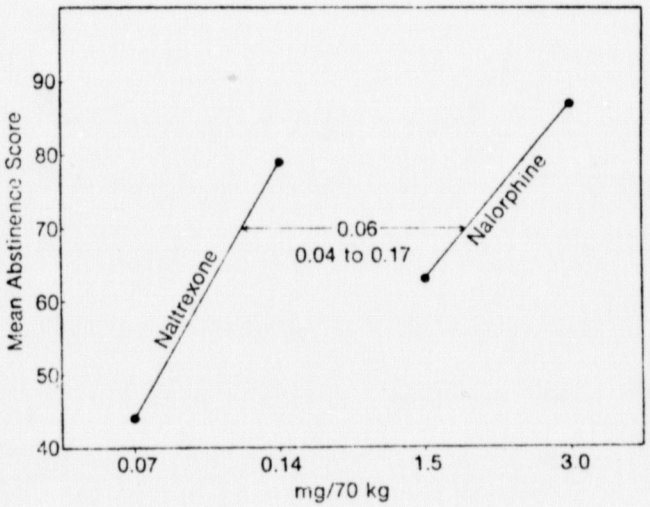
Table 1.—Effects of Naltrexone (30 mg orally) on Physiologic Changes and Subjective State*

	Vehicle	Naltrexone	Difference
Systolic blood pressure	23.4	51.1	27.7
Diastolic blood pressure	1.6	31.6	30.0[.05]
Pupillary diameter	2.6	1.0	− 1.6
Temperature	2.1	1.0	− 1.1[.05]
Pulse rate	9.6	12.4	2.8
Respiratory rate	6.2	1.0	− 5.2
Opiate signs	4.6	3.2	− 1.4
Opiate symptoms	0.2	2.0	1.8
Liking—observers	1.2	1.2	0
Liking—patients	0	0	0
LSD†	26.4	27.3	0.9
MBG†	0	1.2	1.2
PCAG†	25.6	23.2	2.4

* Each value is the mean, for five subjects, of the sum of the differences between the mean control value and the treatment values or the sum of observations for the first 5 hours after drug administration. The superscripts indicate those differences that were statistically significant at the .05 level.

† LSD is the LSD scale; MBG is the morphine-benzadrine group scale which measures feelings of euphoria and well-being; and PCAG is the pentobarbital-chlorpromazine-alcohol group scale which measures feelings of apathetic sedation.[7]

Fig 3.—Potency and 95% confidence limits of naltrexone relative to nalorphine in precipitating abstinence in six subjects dependent on 60 mg of morphine daily. Relative potency and confidence limits are expressed as mg naltrexone equivalent to 1 mg of nalorphine.



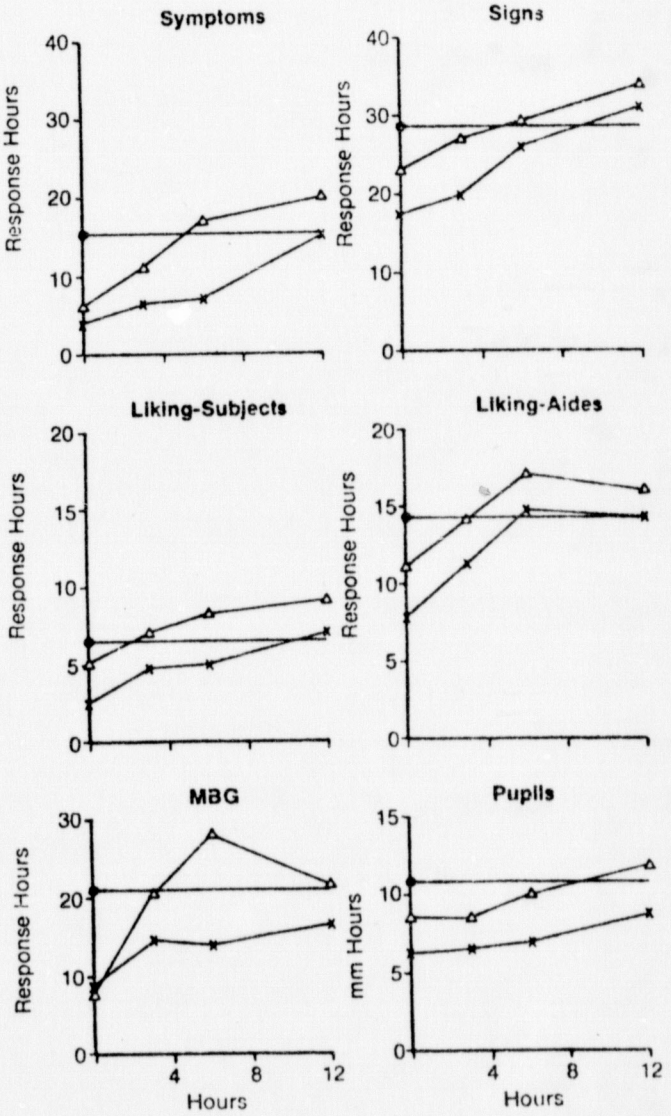


Fig 4.—Comparison of time-action courses of naloxone and naltrexone in antagonizing pupillary constrictive and subjective changes produced by morphine. Solid dots and horizontal lines indicate effects of 25 mg/70 kg of morphine. Triangles indicate effects of naloxone (1 mg) administered with morphine, and 3, 6, and 12 hours before. Crosses indicate alterations in morphine effect produced by naltrexone (0.5 mg), administered with or 3, 6, or 12 hours before morphine. Each point represents mean of sum of responses or differences between responses obtained during first five hours after administration of morphine.

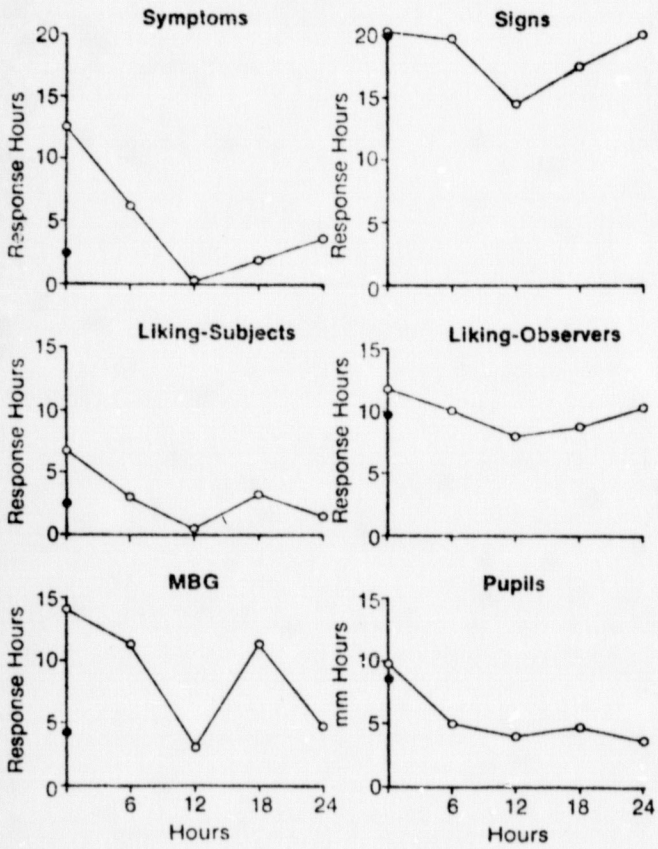


Fig 5.—Effects of orally administered naltrexone (15 mg) on response to 30 mg of morphine administered subcutaneously. Naltrexone was administered 6, 12, 18 and 24 hours before morphine. Open circles on ordinant indicate effects of 30 mg; closed circles, of 15 mg of morphine. Each point represents mean of sum of scores or differences obtained for first five hours after administration of morphine in five subjects.

Table 2.—Effects of Chronically Administered Naltrexone (15 mg Twice a Day Orally) on Subcutaneously Administered Morphine*

	Control		Naltrexone	
Dose of Morphine (mg)	15	30	50	100
Feel effect—patients	2.4	4.9	0.4	0.7
Feel effect—observers	5.9	5.7	5.3	3.3
Identification—patients	1.3	3.5	0	0
Identification—observers	5.6	5.7	5.1	3.3
Symptoms	2.6	19.6	0.3	0.7
Signs	12.7	20.4	15.7	11.4
Liking—patients	2.5	9.7	0	0.7
Liking—observers	6.6	11.6	7.3	4.9
MBG scale	4.3	14.0	2.9	2.6
Pupils	8.6	9.8	1.9	4.2

* Each value represents the mean, for six subjects, of the sum of responses for the first five hours after the administration of morphine for subjective responses. For pupils the mean is for the sum of the differences between the mean control value and the observations for the five-hour period following the administration of morphine.

morphine. These dose levels were adjudged to be equipotent on the basis of their ability to precipitate abstinence. In subjects dependent on 240 mg of morphine, naloxone was seven times as potent as nalorphine.[7] Recent estimates of naloxone's potency relative to nalorphine in subjects dependent on 60 mg of morphine indicate that it is ten times as potent as nalorphine[10]; thus, naloxone would be estimated to be 0.6 times as potent as naltrexone. As can be seen, the degree of blockade produced by naltrexone was greater than that of naloxone at all times and the half life of naltrexone blockade was at least twice that of naloxone.

The blockade produced by a single 15-mg oral dose of naltrexone is evident six hours after administration, becomes maximal by 12 hours, and persists for over 24 hours (Fig 5).

Blocking Action of 15 and 25 mg of Naltrexone Administered Chronically.—As can be seen from Table 2, by all measures the effects of 100 mg of morphine in subjects receiving naltrexone, 15 mg twice a day orally, were less than those of 15 mg of morphine in these subjects prior to receiving naltrexone. Observers and subjects were not able to differentiate 50 and 100 mg of morphine in patients receiving naltrexone; however, the effect of these doses was distinguishable on pupils. Similar observations were made in subjects receiving 50 mg of naltrexone daily. The pupillary data suggest that 15 mg of naltrexone administered twice daily attenuates the effects of morphine by a factor of 20. Fig 6 illustrates the effects of chronically administered morphine (240 mg/day) in patients receiving naltrexone (30 and 50 mg a day orally) as assessed by the modified chronic-dose questionnaire. Only one subject identified his medication as a narcotic and then only on two occasions. Six of the patients did not recognize or identify effects of the medication, while the other three on various occasions identified their medication as a barbiturate, amphetamine, chlorpromazine, or a minor tranquilizer (meprobamate or chlordiazepoxide). On some days these patients made several different identifications. In contrast, the observers commonly identified the drug as a narcotic even through the third day of withdrawal. Whereas the observers thought the patients liked the medication and that it made the patients feel good, the patients reported a mild aversion toward morphine. At least a partial explanation of this disparity was due to the fact that some patients experienced mild abstinence symptoms shortly following the ingestion of naltrexone and thought they were "kicking." When morphine was withdrawn, about 50% of the patients recognized that they were abstinent. Although the observers thought all patients were "hooked" and abstinent when morphine was withdrawn, they did not recognize that the patients were kicking until the third day of abstinence. Although patients reported that they felt slightly to moderately bad when they were withdrawn, they did not appear sick.

Figure 7 illustrates the intensity and time course of abstinence in patients dependent on 240 mg/day of morphine who had been treated with naltrexone and cyclazocine,[7] as well as a group of untreated patients.[12] As can be seen, both the 30 and 50 mg daily doses of naltrexone markedly attenuated the degree of abstinence and dependence. The

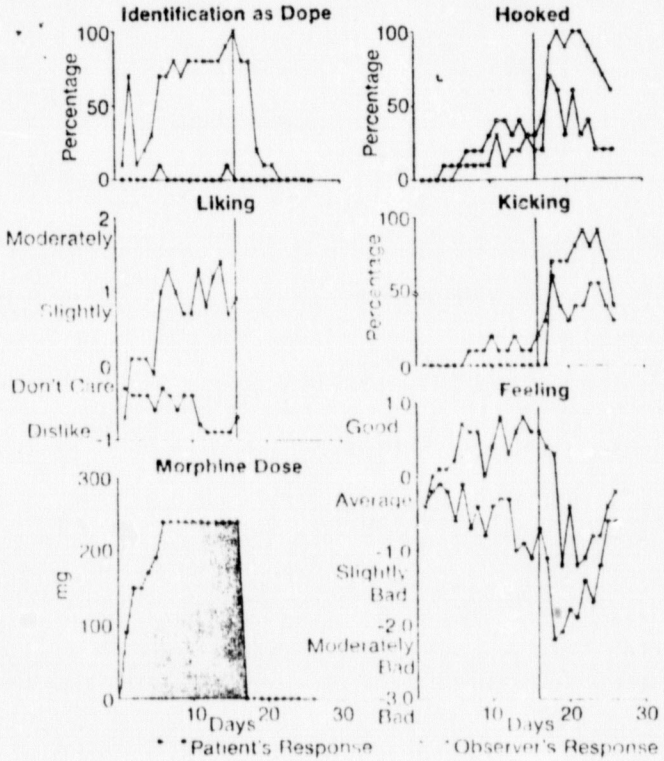


Fig 6.—Changes reported by patients and observers on chronic dose questionnaire during a cycle of morphine dependence in subjects receiving naltrexone chronically. Each point represents mean response of nine subjects who had received naltrexone in dose levels of either 15 or 25 mg twice daily, or 50 mg once daily.

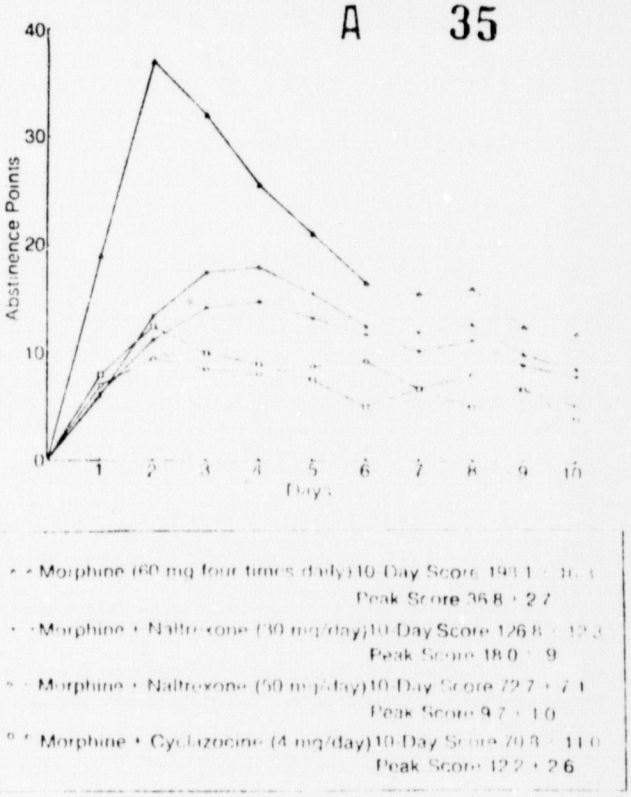


Fig 7.—Effects of chronically administered naltrexone and cyclazocine on abstinence scores following abrupt withdrawal of patients made dependent on 240 mg of morphine per day. (Data for morphine alone from Fraser et al.[3]; for cyclazocine (open squares), from Martin et al.[2]) Line joining solid circles is mean of abstinence scores for all patients who received either naltrexone in dose levels of 30 or 50 mg/day.

30-mg dose level was less efficacious than the cyclazocine (2 mg twice daily), whereas, 50 mg of naltrexone produced a comparable degree of blockade.

Comment

Naltrexone is a potent narcotic antagonist. In man it appears to be 17 times more potent than nalorphine, which would make it approximately twice as potent as naloxone. These findings agree well with those reported by Blumberg et al[10,11] in rats, mice and rabbits. In the morphine-dependent dog, naltrexone is 2.5 (1.8 to 3.8) times more potent than naloxone in precipitating abstinence. Further, its duration of action is appreciably longer than that of naloxone *in man*. Blumberg and Dayton[11] reported that naltrexone had a slightly longer duration of action than naloxone in rodents. The fact that the methylcyclopropyl substitution on the nitrogen markedly enhances the duration of antagonistic action of this oxymorphone antagonist is similar to the observations made with the similarly substituted benzomorphan cyclazocine,[2] suggesting that the congeners with the N-methylcyclopropyl moiety are metabolized or distributed quite differently in man than they are in rodents and the dog.[11] Finally, naltrexone is effective orally in man as an antagonist in modest dose levels (30 to 50 mg/day). Much larger doses of naloxone (up to 3,000 mg/day) are required to produce a comparable level of blockade.[8] Indeed, 50 mg of naltrexone a day orally produces a level of antagonism in preventing the development of physical dependence on morphine in man that is comparable to that produced by 4 mg orally a day of cyclazocine.[2]

If naltrexone has agonistic activity of either the nalorphine type or morphine type, they are minimal. In dose levels that are adequate for blockade, patients have not reported subjective changes that are different than those seen under placebo conditions. On the other hand, 30 mg orally of naltrexone produced a significant increase in diastolic blood pressure and perhaps some pupillary constriction.

Blumberg and Dayton[11] have reported that naltrexone has liminal analgesic action in the rat, but not the mouse, using the phenylquinone writhing test. We have not been able to detect significant agonistic actions of naltrexone in the chronic spinal dog and if they are present, they are highly variable. As indicated, only one patient who received 70 mg of naltrexone subcutaneously exhibited a syndrome which resembled in any way the type of psychotomimetic and dysphoric reactions seen with cyclazocine and nalorphine. It is within the realm of possibility that naltrexone can be partially metabolized to an active compound by some species and individuals.

In some patients, the administration of naltrexone, particularly large doses, evoked reports of yawning and stretching. It is not known whether these signs and re-

ports are meaningful actions of naltrexone or are signs of precipitated protracted abstinence.

No change in signs or symptoms was seen when naltrexone was discontinued following its chronic administration at either the 30 or 50 mg daily dose level. When patients were stabilized on both naltrexone and morphine, the patients indicated an unplesant state to which they expressed a slight aversion. This observation demonstrates that the chronic administration of naltrexone effectively antagonizes the euphorogenic effects of morphine. Two factors may contribute to the patients' negative reaction to the administration of both naltrexone and morphine chronically: (1) When subjects were stabilized on morphine, the ingestion of naltrexone would precipitate mild signs and symptoms of abstinence which would become manifest within 15 to 30 minutes and would subside over the following hour. (2) The fact that the patients did not experience euphoria with the administration of morphine was a disappointment to them.

It would appear that a single daily dose of naltrexone does not provide quite the same sustained level of blockade that is attained with cyclazocine; however, this probably would be of little clinical significance since it is unlikely that patients would wish or be able to use the quantity of narcotics chronically on the street that were employed in this study. Further, the lack of agonistic effects of naltrexone may be in most treatment conditions more than an offsetting advantage. Because of its potency and longer duration of action and oral effectiveness, naltrexone has definite advantages over naloxone in the treatment of heroin dependence.

A preliminary report of these data was presented at the 74th annual meeting of the American Society for Clinical Pharmacology and Therapeutics, New Orleans, March 23, 1973.

References

1. Martin WR, et al: Studies of the dependence-producing potential of the narcotic antagonist 2-cyclopropylmethyl-2'-hydroxy-5,9-dimethyl-6,7-benzomorphan (cyclazocine, Win 20,740, ARC II-C-3). *J Pharmacol Exp Ther* 150:426-436, 1965.
2. Martin WR, Gorodetzky CW, McClane TK: An experimental study in the treatment of narcotic addicts with cyclazocine. *Clin Pharmacol Ther* 7:455-465, 1966.
3. Martin WR, Gorodetzky CW: Cyclazocine, an adjunct in the treatment of narcotic addiction. *Int J Addict* 2:85-93, 1967.
4. Martin WR: A homeostatic and redundancy theory of tolerance and dependence to narcotic analgesics, in Wikler A (ed): *The Addictive States*. Baltimore, Williams & Wilkins Co, 1968, pp 206-225.
5. Jaffe JH, Brill L: Cyclazocine, a long-acting narcotic antagonist: Its voluntary acceptance as a treatment modality by narcotics abusers. *Int J Addict* 1:99-123, 1966.
6. Freedman AM, et al: Cyclazocine and methadone in narcotic addiction. *JAMA* 202:191-194, 1967.
7. Jasinski DR, Martin WR, Haertzen CA: The human pharmacology and abuse potential of N-allylnoroxymorphone (naloxone). *J Pharmacol Exp Ther* 157:420-426, 1967.
8. Zaks A, et al: Naloxone treatment of opiate dependence; a progress report. *JAMA* 215:2108-2110, 1971.
9. Blumberg H, Pachter IJ, Matossian Z: US Pat 3, 332, 950, July 25, 1967.
10. Blumberg H, Dayton HB, Wolf PS: Analgesic and narcotic antagonist properties of noroxymorphone derivatives. *Toxicol Appl Pharmacol* 10:406, 1967.
11. Blumberg H, Dayton HB: Narcotic antagonist studies with EN-1639A (N-cyclopropylnoroxymorphone hydrochloride), in *Fifth International Congress on Pharmacology. Abstracts of Volunteer Papers*. The Congress, 1972, p 23.
12. Fraser HF, et al: Methods for evaluating addiction liability: (A) "Attitude" of opiate addicts toward opiate-like drugs; (B) A short-term "direct" addiction test. *J Pharmacol Exp Ther* 133:371-387, 1961.
13. Jasinski DR, Martin WR, Sapira JD: Antagonism of the subjective, behavioral, pupillary and respiratory depressant effects of cyclazocine by naloxone. *Clin Pharmacol Ther* 9:215-222, 1968.
14. Finney DJ: *Experimental Design and its Statistical Basis*. Chicago, University of Chicago Press, 1955.
15. Himmelsbach CK: Clinical studies of drug addiction. II. "Rossium" treatment of drug addiction. *Public Health Rep*, suppl 125, 1937.
16. Jasinski DR, Martin WR, Hoeldtke R: Studies of the dependence-producing properties of GPA-1657, profadol and propiram in man. *Clin Pharmacol Ther* 12:613-649, 1971.
17. McClane TK, Martin WR: Effects of morphine, nalorphine, cyclazocine and naloxone on the flexor reflex. *Int J Neuropharmacol* 6:89-98, 1967.
18. Martin WR, Jasinski DR: Characterization of EN-1639A (N-cyclopropylmethyl-7,8-dihydro-14-hydroxynormorphinone HCl), a narcotic antagonist. *Clin Pharmacol Ther* 14:142, 1973.

FURTHER ANSWERS TO INTERROGATORIES

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

x U.S. DISTRICT COURT FILED 4-20-73 S.D. of N.Y.

OTIS CLAY,

Plaintiff,

-v-

DR. MARTIN, et al., and THE UNITED STATES GOVERNMENT, Washington, D. C.,

Defendants.

71 Civ. 2306 S.J.R.

FURTHER ANSWERS TO INTERROGATORIES

x

Defendants, by their attorney, Paul J. Curran, United States Attorney for the Southern District of New York, hereby provide further answers to plaintiff's Interrogatories, dated August 3, 1973, without waiving any objection to said Interrogatories:

1. In response to interrogatory 6 and further response to interrogatories 5 and 9 defendants herewith provide to plaintiff copies of the following publications relating to drug EN-1639A:

(a) Narcotic Antagonist Studies with EN-1639A, etc.

(b) Analgesic and Narcotic Properties of Noroxymorphone Derivatives

(c) Characterization of N-cyclopropylmethyl-7, 8-dihydro-14-hydroxynormorphine-HCl, a narcotic antagonist

(d) Human Metabolite of Naltrexone etc.

(e) Characteristics of the Blocking Effects of EN-1639A etc.

Dated: New York, New York

November 16, 1973

Yours, etc.

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Southern District of New York
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137 NARCOTIC ANTAGONIST STUDIES WITH EN-1639A (N-CYCLOPROPYL-METHYLNOROXYMORPHONE HYDROCHLORIDE). Harold Blumberg and Hyman B. Dayton. Endo Laboratories, Inc., Garden City, N.Y. 11530, USA

In narcotic antagonist studies in mice, rats, and rabbits, EN-1639A (N-cyclopropylmethylnoroxymorphone HCl) is about twice as active as naloxone (N-allylnoroxymorphone) HCl by S.C. injection, and slightly longer-acting. However, EN-1639A shows slight agonist action, as indicated by limited analgesic activity S.C. on the phenylquinone test in rats, whereas naloxone does not. Orally EN-1639A is about 8 times as active as and about 3 times as long-acting as naloxone in narcotic antagonism in rats. EN-1639A has now been compared also with the potent veterinary narcotic antagonist, diprenorphine HCl (M5050). In the S.C. prevention of oxymorphone (OM) Straub tail in mice, EN-1639A and M5050 were essentially equal, with ED50 ± S.E. values of: EN-1639A .0133 ± .0037, M5050 .0118 ± .0020 mg/kg. By counteraction of OM narcosis S.C. in rats, they were also equal, ED50 ± S.E. figures being: EN-1639A .028 ± .001, M5050 .034 ± .007 mg/kg. Likewise, in oral counteraction of OM narcosis in rats, EN-1639A and M5050 were equal in activity and duration of action. In the phenylquinone test for analgesia in mice, M5050 was inactive, like naloxone and EN-1639A. However, in the phenylquinone test in rats M5050 showed limited analgesic agonist action S.C., like EN-1639A, in contrast to the "purer" antagonist, naloxone, which showed no analgesic or agonist action. The limited analgesic activity of M5050 in the rat was counteracted by naloxone.

In: Fifth International Congress on Pharmacology, Abstracts of Volunteer Papers. The Congress, 1972, p. 23.

74. *Analgesic and Narcotic Antagonist Properties of Noroxymorphone Derivatives.* H. Blumberg, H. B. Dayton, and P. S. Wolf, Endo Laboratories, Garden City, New York.

Oxymorphone, or 14-hydroxydihydromorphinone, is a potent narcotic analgesic. However, the *N*-allyl derivative, naloxone, is a potent narcotic antagonist that is about 15–30 times as active as the widely used nalorphine in both animals and man. Three newly synthesized derivatives of noroxymorphone have now been investigated for analgesic activity by the phenylquinone writhing test in rats and for narcotic antagonist activity by the counteraction of oxymorphone narcosis in rats. The compounds were injected subcutaneously as the water-soluble hydrochlorides. *N*-3',3'-Dimethylallylnoroxymorphone was a moderately active analgesic, and about one-half as active as nalorphine as a narcotic antagonist. *N*-Cyclopropylmethylnoroxymorphone had limited effectiveness as an analgesic, but was an extremely potent narcotic antagonist, about 39 times as active as nalorphine. *N*-Cyclobutylmethylnoroxymorphone was a potent analgesic and at the same time a potent narcotic antagonist, being about 5 times as active as nalorphine. It is interesting that the analgesic activity of the three new narcotic antagonists could be counteracted by the other narcotic antagonist, naloxone. *N*-Cyclopropylmethylnoroxymorphone appears to be one of the most potent narcotic antagonists derived from the morphine and morphinone chemical series.

Toxicol. Appl. Pharmacol. 10:406, 1967.

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Clinical Pharmacology and Therapeutics:
Vol. 14:(1) 142, 1973.

Characterization of N-cyclopropylmethyl-7,8-dihydro-14-hydroxynormorphine HCl, a narcotic antagonist.

W. R. Martin, M.D., and D. P. Jasinski, M.D., NIMH Addiction Research Center, Lexington.

This antagonist, EN-1639A, was investigated in man as part of an effort to obtain a potent long-lasting narcotic antagonist devoid of undesirable side effects, which would have utility in the treatment of heroin addicts. The potency of EN-1639A (0.07 and 0.14 mg/70 kg) as a morphine antagonist in comparison with nalorphine (1.5 and 3.0 mg/70 kg) was assessed by its ability to precipitate abstinence in patients dependent on 60 mg of morphine a day. EN-1639A was found to be 17 times more potent than nalorphine. The duration of action of both EN-1639A (0.5 mg/70 kg) and naloxone (1.0 mg/70 kg) was assessed by administering these antagonists subcutaneously with and 3, 6, and 12 hours prior to 30 mg of morphine. EN-1639A has a longer duration of action than naloxone but not as long as cyclazocine. EN-1639A (15 mg) administered orally antagonized morphine (30 mg) for over 24 hours. Further, when EN-1639A was administered chronically either in dose levels of 15 or 25 mg twice daily orally or once daily orally in a dose of 50 mg, it markedly attenuated the degree of physical dependence produced by the chronic administration of morphine (60 mg q.i.d.). These dose levels of EN-1639A were not associated with undesirable side effects. EN-1639A appears to have potential for the treatment of heroin dependence.

PEP/LVFT. Decreases in diastolic pressure, and increases in systolic and pulse pressure were the same for both doses, and mean blood pressure dropped only slightly. Saline infusion resulted in no significant changes. Both methoxamine and isoproterenol caused nearly equal increases of 100% (for the low dose) and 150% (for the higher dose) in peripheral renin activity, as measured by radioimmunoassay. Thus, both alpha and beta stimulation resulted in similar renin release, suggesting a lack of receptor or hemodynamic specificity of renin response.

Presented at annual meeting of American Society for Clinical Pharmacology and Therapeutics, New Orleans, La., March 1973

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HUMAN METABOLITE OF NALTREXONE (N-CYCLOPROPYLMETHYLNOROXYMORPHONE) WITH A NOVEL C-6 ISOMORPHINE CONFIGURATION

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(Received in USA 18 April 1973; received in UK for publication 4 June 1973)

Naltrexone I (1) like naloxone II (2) has been reported to be a potent narcotic antagonist with little or no agonistic effects. Since naltrexone is more potent than naloxone and has a greater duration of action in man (3) and in rodents (4) it was felt that its mode of

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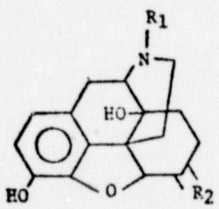
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I; R_1 = CH_2-cyclopropyl, R_2 = O

II; R_1 = $CH_2CH{=}CH_2$, R_2 = O

III; R_1 = CH_2-cyclopropyl, R_2 = H, OH

IV; R_1 = CH_2-cyclopropyl, R_2 = OH, H

metabolism and rate of excretion of metabolites were of interest as possible explanations of these differences. Naloxone has been reported to be metabolized in man by glucuronidate conjugation (5) N-dealkylation (6) and reduction of the C-6 carbonyl to form N-allyl-7,8-dihydro-14-hydroxynormorphine (6). No metabolic data has been reported for naltrexone.

The subjects in this study were healthy, adult, male federal prisoner volunteers; all are former narcotic addicts who were incarcerated at the NIMH Addiction Research Center at the time of the study. Urine from two subjects receiving 50 mg/day of naltrexone orally for approximately six weeks (and free from other drugs) was collected ad lib and every eight hours for two days. Three subjects received a single oral dose of naltrexone, 50 mg, and urine was collected as described above.

Urine samples from the chronic subjects which were richest in metabolite (as monitored by tlc comparison with authentic III) were extracted with chloroform after adjustment of

pH to 9.5 with sodium hydroxide and phosphate buffer. Evaporation of solvent gave ~4 mg of brown residue. Preparative tlc of the zone corresponding to III (elution on silica gel-benzene:diethylamine (4:1) followed by elution on Gelman type SG fiber glass sheets-chloroform saturated with ammonia (5)) gave a substance which was visualized with potassium iodoplatinate spray as a single spot on both systems. Treatment of an ether extract of the substance with dry hydrogen chloride gave a fluffy white precipitate which was washed with ether and dried (~0.2 mg) (7). Silylation of a portion of the metabolite and III with BSTFA (10% TMCS) (8) in acetonitrile (1:1) in a sealed tube at 70°C for one hour followed by injection on gc (3% OV-17 on GCQ, 2 mm x 6 ft. glass, 270°C, f.i.d. 275°C) gave a major peak with uncorrected R_t = 5.10 min. for the metabolite and 5.55 min. for III (9).

Spectral data on the metabolite, I and III are given in the Table. The excitation and emission spectra of the metabolite and III indicate a similar but nonidentical structural relationship. The lack of a carbonyl absorption coupled with the molecular weight of 343 for the metabolite support assignment of structure IV, the C-6 epimer of III.

TABLE

Spectral Characteristics of the Metabolite, I and III

Metabolite	III	I	Type of Analysis
247, 277, 318 417	249, 278, 320 427	-[d]	Fluoresence[a] Excitation (nm) Emission (nm)
3450 -	3450 -	3450(OH) 1730(C=O)	Infrared[b] (cm^{-1})
M^+343(100) M^+-41(43) M^+-55(23)	M^+343(36) M^+-41(16) M^+-55(10)	M^+341(9) M^+-41(37) M^+-55(31)	Mass Spectra[c]

[a] Values represent λ max, uncorrected with quinine sulfate standard. Samples were developed on silica gel (chloroform saturated with ammonia), sprayed with ferri-ferrocyanide reagent (10) and eluted with pH 9 phosphate buffer.

[b] KBr

[c] Molecular ion M^+ (% abundance), 70 eV.

[d] No fluoresence observed under these conditions.

In a study of the C-6 configuration of morphine derivatives Sargent, et al. (11) were able to conclude that 14-hydroxycodeine (prepared by sodium borohydride reduction of 14-hydroxycodeinone) had the C-6 codeine configuration (α-hydroxy) since similar reduction of

codeinone gave a quantitative yield of codeine (12). In addition Weis and Daum (13) reported that borohydride reduction of dihydro-14-hydroxymorphinone gave dihydro-14-hydroxymorphine without any indication of the C-6 epimer. In the present study sodium borohydride reduction of I in methanolic dioxane resulted in a quantitative yield of III confirming the C-6 morphine configuration of III.

In order to confirm the structural assignment of the metabolite as IV its reactivity was compared to that of III in the Oppenauer reaction. Rapoport, et al. (14) reported in a study of dihydro alcohols of morphine origin in the Oppenauer reaction that the cis-alcohol (C-6 α-hydroxy) is more easily oxidized than the trans (C-6 β-hydroxy) and concluded that the effect was likely due to presence of steric hindrance of the α-substituent to the formation of the pseudo-ring in the case of the trans alcohol vs the cis. Oxidation of III and metabolite with aluminum isopropoxide and cyclohexanone in refluxing benzene (3 hr.) gave 20% and 0% yield of I respectively. Under forcing conditions (potassium t-butoxide and benzophenone in refluxing toluene for 3 hr.) III and the metabolite were oxidized to I in yields of 99% and 74%. The conversion of the metabolite to I establishes the link between the C-6 epimers and confirms the structural assignment of the metabolite as IV. The metabolite also was found in the urine of the single dose subjects.

This is the first reported example of metabolic reduction of a morphine related compound to a metabolite with the C-6 isomorphine configuration. Studies are being continued to assess the pharmacological implications of this metabolite.

Acknowledgements. The author would like to thank Dr. S. Y. Yeh for helpful discussions. Samples of I, II and III were kindly provided by Endo Laboratories, Inc., Garden City, New York. An additional sample of III was provided by Dr. E. L. May, National Institutes of Health, Bethesda, Md.

REFERENCES

1. H. Blumberg, H. B. Dayton and P. S. Wolf, Toxicol. Appl. Pharmacol., 10, 406 (1967).
2. D. R. Jasinski, W. R. Martin and C. A. Haertzen, J. Pharmacol. Exp. Ther., 157, 420 (1967).
3. W. R. Martin, D. R. Jasinski and P. A. Mansky, Arch. Gen. Psychiat. (1973), in press.
4. H. Blumberg and H. B. Dayton, Fifth International Congress on Pharmacology, Abstracts of Volunteer Papers, 23 (1972).

5. J. M. Fujimoto, Proc. Exp. Biol. Med., 133, 317 (1970)

6. S. H. Weinstein, M. Pfeffer, J. M. Schor, L. Indindoli and M. Mintz, J. Pharm. Sci., 60, 1567 (1971).

7. A sufficient amount of metabolite was not isolated to permit elemental analysis.

8. Bis-(trimethylsilyl)-trifluoroacetamide (10% trimethylchlorosilane) obtained from Regis Chemical Co., Morton Grove, Illinois.

9. The retention times remained unchanged when cochromatographed. Gc analysis of control urine collected prior to drug administration was negative.

10. H. Kupferberg, A. Burkhalter and E. L. Way, J. Chromatogr., 16, 558 (1964).

11. L. J. Sargent, L. H. Schwartzman and L. F. Small, J. Org. Chem., 23, 1247 (1958).

12. M. Gates, J. Am. Chem. Soc., 75, 4340 (1953).

13. U. Weiss and S. J. Daum, J. Org. Chem., 8, 123 (1965).

14. H. Papoport, R. Naumann, F. P. Bissell and R. M. Bonner, J. Org. Chem., 15, 1103 (1950).

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In: National Research Council-Problems of drug dependence, Vol. 1:179-191, 1971. Presented at 33rd Annual Scientific Meeting, Committee on Problems of Drug Dependence, Toronto, 1971.

CHARACTERISTICS OF THE BLOCKING EFFECTS OF EN-1639A

(N-CYCLOPROPYLMETHYL-7,8-DIHYDRO-14-HYDROXYNORMORPHINONE HCl)

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Health Services and Mental Health Administration

Several years ago while studying the narcotic antagonist cyclazocine, it was found that tolerance developed to its agonistic activity but not to its antagonistic activity. It was further observed that cyclazocine was orally effective and had a long duration of action. These findings suggested that it would be possible to maintain former narcotic dependent subjects on a dose of an antagonist that would prevent narcotics from exerting their euphorogenic and dependence-producing effects, and thus, provide a circumstance where both physiological and conditioned behavior related to drug acquisition and to relapse could be extinguished. Early studies of Jaffe and Brill (1966) and Freedman et al. (1967) indicated that select patients might indeed be helped by narcotic antagonists; however, the unpleasant agonistic effects of cyclazocine made stabilization on blocking doses difficult, and the fact that an effective blockade could be maintained for only 24 hours with a daily oral dose was not only an inconvenience for the patient but allowed the effects of narcotics to become manifest by omitting a single dose. In an extensive series of studies in man, the narcotic antagonist naloxone was found to be virtually devoid of agonistic activity (Jasinski et al., 1967); however, it had a relatively short duration of action. Fink et al. (1968) have been able, using very large doses of naloxone, to attain effective blockade of morphine for nearly 24 hours. It has been the general consensus of investigators

such as Jaffe, Freedman and Fink that for a narcotic antagonist to be optimally effective in the ambulatory treatment of narcotic addicts it must be administered in such a way that its effects would have an appreciable duration of action (one week to one month), that it should be devoid of agonistic activity, and that it should be a highly potent compound to permit its administration in a depot form.

Cyclazocine, which has an N-methyl substitution on the nitrogen, has exhibited an exceedingly long duration of action in man. On the assumption that its long duration of action was related to the substitution on nitrogen, we felt that it would be worthwhile to study the N-cyclopropylmethyl congener of naloxone. This compound, EN-1639A, was synthesized in the research laboratories of Endo Pharmaceuticals (Blumberg, Pachter and Matossian). Blumberg et al. (1967) briefly characterized some of the pharmacological properties of EN-1639A and have subsequently intensively studied the compound in animals. Their findings indicated that EN-1639A was nearly twice as potent as naloxone as an antagonist, that it had only slightly agonistic activity (e.g., analgesia), and that it had a longer duration of action than naloxone.

The preliminary results reported in this communication will summarize our findings to date with this compound in man.

Dose ranging

Dose levels from 0.01 to 80 mg of EN-1639A subcutaneously and 0.5 to 100 mg orally were studied in 10 subjects. A variety of subjective effects were reported which included turning of the stomach, nausea and in one instance vomiting, tiredness, relaxation, sleepiness, coasting, a syndrome to which the patients refer as the "stretches" in which they yawned and stretched, racing thoughts, irritability, and an anxiety reaction in one patient who received 70 mg of EN-1639A subcutaneously. Another patient who received 80 mg of EN-1639A subcutaneously reported no changes. Regression analysis for a variety of parameters revealed that only pupillary constriction was related to dose; however, there was a trend for blood pressure to be somewhat elevated. In a study of 5 patients in whom the effects of 30 mg of EN-1639A administered orally were compared with the effects of a comparable placebo, it was found that diastolic blood pressure was elevated approximately 5 or 6 mm, and this difference was statistically significant. There was also a very small but statistically significant fall in body temperature. In apparent contrast to the dose run-up, EN-1639A did not cause a statistically significant degree of pupillary constriction.

Relative potency of EN-1639A in man

The potency of EN-1639A in precipitating abstinence in patients physically dependent on 15 mg of morphine administered q.i.d. was studied in 5 patients. Doses of 0.7 and 0.14 mg/70 kg of EN-1639A were compared with 1.5 and 3.0 mg of nalorphine. As can be seen in Fig. 1, EN-1639A is almost 17 times as potent (6-25, 95% confidence limits) as nalorphine, and thus, is over twice as potent as naloxone. These findings are in close agreement with those made by Blumberg and his collaborators in animals.

Duration of action of EN-1639A

A comparison of EN-1639A administered subcutaneously with naloxone administered subcutaneously. EN-1639A (0.5 mg) and naloxone (1.0 mg) were administered subcutaneously, simultaneously with and 3, 6 and 12 hours prior to the administration of 30 mg of morphine subcutaneously in 5 subjects. Pupillary diameter was determined photographically, and subjective effects were measured using standard questionnaires. As can be seen in Fig. 2, EN-1639A produced a marked antagonism of the effects of morphine, and the effects persisted for many hours longer than the effects of naloxone. By way of comparison, data previously acquired in a study of cyclazocine (0.6 mg/70 kg) indicate that the action of a dose of cyclazocine which would be approximately equipotent

to 1 mg of naloxone was greater and of a longer duration of action than EN-1639A.

Effects of EN-1639A administered orally. In another study, the effects of 15 mg of EN-1639A administered orally 6, 12, 18 and 24 hours prior to the administration of 30 mg of morphine administered subcutaneously were studied in 6 subjects. The blocking effects on the miotic effects of morphine are presented in Fig. 3. As can be seen, this dose of EN-1639A orally produced blockade that persisted for over 24 hours.

The effects of chronically administered EN-1639A on the dependence-producing effects of morphine

EN-1639A was administered twice daily to 6 patients. On day 1 they received 7.5 mg b.i.d., day 2, 10 mg, and day 3, and thereafter, 15 mg. When stabilized on 15 mg b.i.d. they first received 50 and then 100 mg of morphine subcutaneously. The effects of these doses of morphine were quite modest and were of the same order of magnitude as effects obtained in comparable experiments conducted with cyclazocine. Following these two doses of morphine, patients received 100, 140, 180 and then 240 mg of morphine daily administered in four equally divided doses. Having reached a stabilization dose on the fourth day of chronic administration, they were then stabilized for 14 days. During the

stabilization period, minor morphine-like effects were observed in some patients. Further, several patients claimed that with the administration of the morning and evening doses of EN-1639A they developed a mild abstinence syndrome. This was investigated systematically, and there were no objective signs of abstinence seen in the patients at the time they reported symptoms. Following stabilization, the patients were abruptly withdrawn. A summary of the abstinence scores is presented in Fig. 4. As can be seen, EN-1639A produced a definite suppression of the degree of physical dependence; however, the dependence was greater as measured by both 10 day and peak abstinence scores than the degree of dependence seen in patients treated with cyclazocine (2 mg every 12 hours).

Summary and conclusions

It would thus appear that EN-1639A is twice as potent as naloxone and cyclazocine as an antagonist. Its duration of action is longer than that of naloxone; however, it is shorter than that of cyclazocine. It probably has agonistic activity of the nalorphine type, namely, it elevates blood pressure, constricts pupils and produces racing thoughts and irritability, as well as other psychotomimetic effects; however, in this regard its activity is much less than that of cyclazocine. The efficacy of EN-1639A by the oral route

is considerably greater than that of naloxone but less than that of cyclazocine. To produce a degree of antagonism that would be equivalent to that of 4-8 mg of cyclazocine daily, a daily dose of 50 to 100 mg of EN-1639A will probably have to be administered. The feasibility of administering this dose will have to be investigated; however, because of the great potency of EN-1639A, it is entirely conceivable that this agent could be administered in a depot which could provide blockade for a week or more.

References

1. Blumberg, H., Dayton, H. B. & Wolf, P. S. Analgesic and narcotic antagonist properties of noroxymorphone derivatives. Toxicol. Appl. Pharmac. (1967) 10: 406.

2. Fink, M., Zaks, A., Sharoff, R., Mora, A., Bruner, A., Levit, S. & Freedman, A. M. Naloxone in heroin dependence. Clin. Pharmac. Ther. (1968) 9: 568-577.

3. Fraser, H. F., Van Horn, G. D., Martin, W. R., Wolbach, A. B. & Isbell, H. Methods for evaluating addiction liability. (A) "Attitude" of opiate addicts toward opiate-like drugs. (B) A short-term "direct" addiction test. J. Pharmac. exp. Ther. (1961) 133: 371-387.

4. Freedman, A. M., Fink, M., Sharoff, R. & Zaks, A. Cyclazocine and methadone in narcotic addiction. J. Am. med. Assoc. (1967) 202: 191-194.

5. Jaffe, J. H. & Brill, L. Cyclazocine, a long-acting narcotic antagonist: Its voluntary acceptance as a treatment modality by narcotics abusers. Int. J. Addict. (1966) 1: 99-123.

6. Jasinski, D. R., Martin, W. R. & Haertzen, C. A. The human pharmacology and abuse potential of N-allylnoroxymorphone (naloxone). J. Pharmac. exp. Ther. (1967) 157: 420-426.

7. Martin, W. R., Gorodetzky, C. W. & McClane, T. K. An experimental study in the treatment of narcotic addicts with cyclazocine. Clin. Pharmac. Ther. (1966) 7: 455-465.

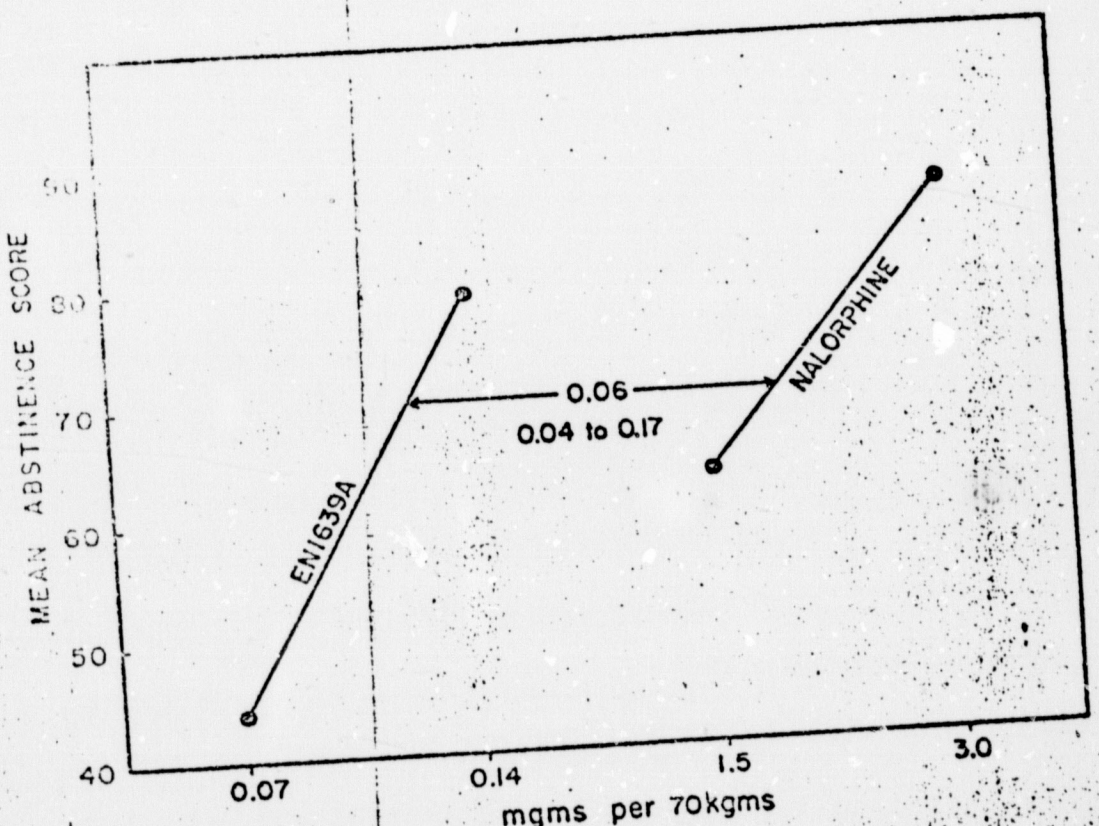


Fig. 1. The potency of EN-1639A relative to nalorphine in precipitating abstinence in subjects dependent on 60 mg of morphine daily.

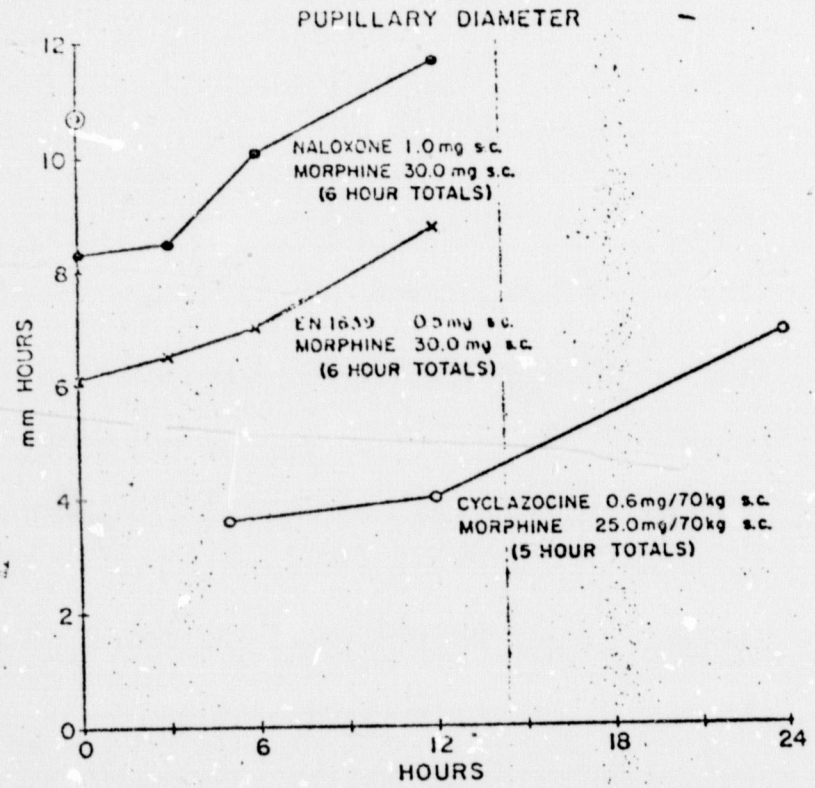


Fig. 2. A comparison of the time action courses of naloxone, EN-1639A and cyclazocine in antagonizing the pupillary constrictive effects of morphine. The experiment with cyclazocine differed from those with naloxone and EN-1639A in that the dose level of morphine was 25 mg/70 kg. The results with cyclazocine were obtained from studies previously reported (Martin et al., 1966). The uppermost dot and open circle on the ordinant are a measure of the constrictive effects of morphine when administered with a placebo. The lower dot and cross on the ordinant are the effects of morphine when administered simultaneously with naloxone and EN-1639A. The remaining symbols are the effects of naloxone, EN-1639A and cyclazocine when administered the indicated number of hours prior to the administration of morphine.

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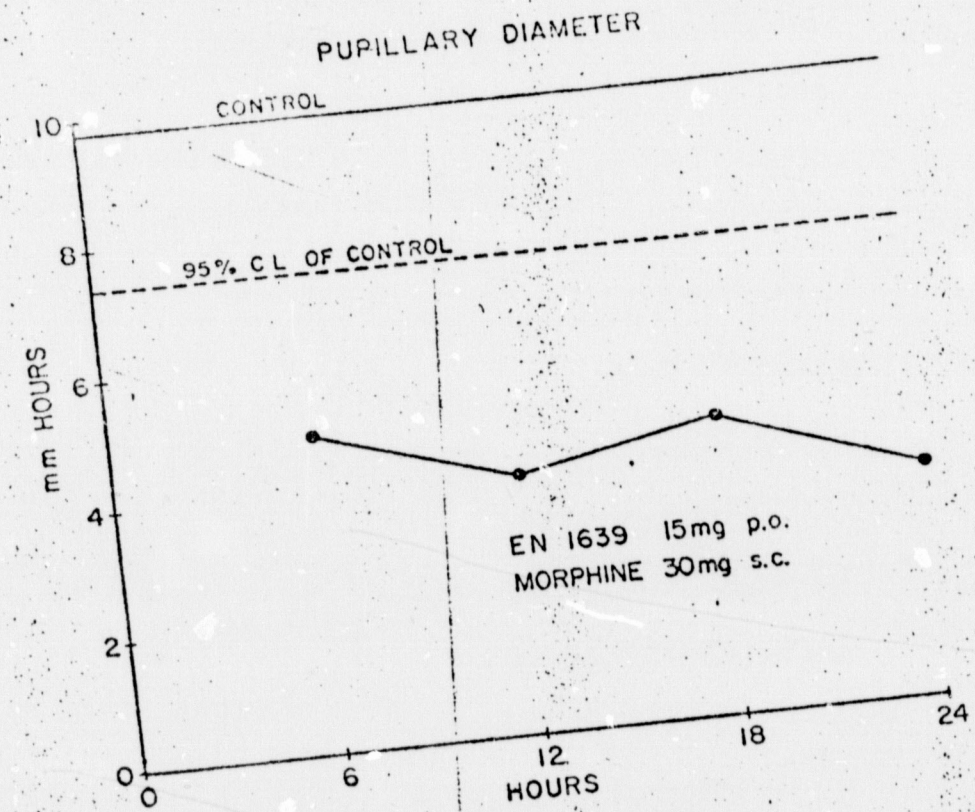


Fig. 3. The duration of action of EN-1639A administered orally as indicated by its ability to antagonize the miotic effect of 30 mg of morphine administered subcutaneously. All points are significantly less than the control value, which represents the effects of morphine when administered with a placebo.

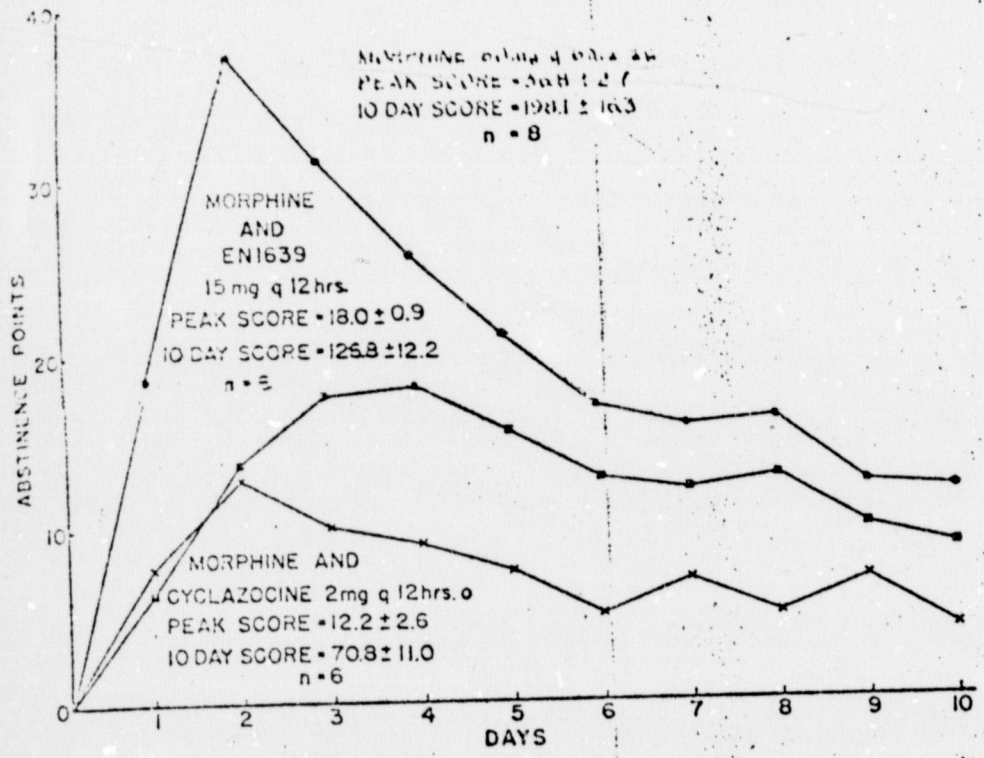


Fig. 4. The ability of cyclazocine and EN-1639A to antagonize the dependence-producing effect of morphine. The upper curve is from an experiment by Fraser et al. (1961) on patients stabilized on 240 mg of morphine daily. The lower curve is from a study on the effects of cyclazocine previously reported (Martin et al., 1966).

ORDER OF RYAN,J., DISMISSING ACTION FOR LACK OF PROSECTION, NOVEMBER 19, 1973

U.S. DISTRICT COURT
FILED
NOV 26 1973
S. D. OF N. Y.

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
Otis Clay
-v-
Dr. Martin, et al.

Docket No. 71 Civ 2306

The above entitled cause having been called on a Special Review Calendar on Nov 19, 1973, under General Rule 23 of this Court, and no one appearing in opposition, it is now Ordered that the above entitled cause be dismissed for lack of prosecution, under said rule, without prejudice and without costs.

Nov 19, 1973
Date: New York, N.Y.

U. S. D. J.

NOV 27 1973

NOTICE OF MOTION FOR RELIEF FROM ORDER OF DISMISSAL

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

- X

OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN, DOCTOR PETER A. MANSKY, and DOCTOR DONALD R. JASINSKI of United States Penitentiary, Lexington, Kentucky

-and-

THE UNITED STATES SURGEON GENERAL, THE UNITED STATES ATTORNEY GENERAL, THE DIRECTOR OF THE BUREAU OF PRISONS, and the UNITED STATES GOVERNMENT, all of Washington, D. C.,

Defendants.

- X

Civil Action No. 2306/71

NOTICE OF MOTION FOR RELIEF FROM ORDER OF DISMISSAL

SIRS:

PLEASE TAKE NOTICE, that upon the affirmation of CARL O. CALLENDER, Esq., dated the 26th day of November, 1973, and upon all prior proceedings had herein, the undersigned will move this Court before JUDGE SYLVESTER J. RYAN at the United States Court House, Foley Square, New York, New York, on the 6th day of December, 1973 at 9:30 o'clock in the forenoon of that day, or as soon thereafter as counsel can be heard, for an order

pursuant to Rule 60 of the Federal Rules of Civil Procedure, 28 U. S. C. setting aside an order of dismissal entered by JUDGE RYAN against the plaintiff upon counsel's failure to appear at a pre-trial conference of which there was no notice, as more fully appears from the affirmation of CARL O. CALLENDER, and Exhibit "A" therein annexed hereto, and further noticing a pre-trial conference pursuant to Rule 16 of the Federal Rules of Civil Procedure, 28 U. S. C., and for such other and further relief as to this Court may seem just and proper.

PLEASE TAKE FURTHER NOTICE that answering affidavits, if any, shall be served upon the undersigned not later than one day before the hearing pursuant to Rule 6 of the Federal Rules of Civil Procedure, 28 U. S. C.

Dated: New York, New York
November 26, 1973

TO: PAUL J. CURRAN
United States Attorney
ATTN: HOWARD S. SUSSMAN
Assistant United States Attorney
Attorney for Defendants
Office & Post Office Address
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

JUDGE SYLVESTER J. RYAN
Clerk of the Court
United States District Court
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

CARL O. CALLENDER, Esq.
Attorney for Plaintiff

Office & Post Office Address
Community Law Offices
176 East 105th Street
New York, New York 10029

H 1 D2

AFFIRMATION OF CARL O. CALLENDER IN SUPPORT OF MOTION FOR RELIEF FROM ORDER OF DISMISSAL

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY, Plaintiff, -against- DOCTOR WILLIAM R. MARTIN, DOCTOR PETER A. MANSKY, and DOCTOR DONALD R. JASINSKI of United States Penitentiary, Lexington, Kentucky -and- THE UNITED STATES SURGEON GENERAL, THE UNITED STATES ATTORNEY GENERAL, THE DIRECTOR OF THE BUREAU OF PRISONS, and the UNITED STATES GOVERNMENT, all of Washington, D. C., Defendants.	Civil Action No. 2306/71 AFFIRMATION IN SUPPORT OF MOTION FOR RELIEF FROM ORDER OF DISMISSAL

STATE OF NEW YORK)
: ss.:
COUNTY OF NEW YORK)

CARL O. CALLENDER, Esq., an attorney duly admitted to practice before the Courts of the State of New York, hereby affirms under penalty of perjury as follows:

1. I am the Director of Community Law Offices, 176 East 106th Street, New York, New York.

2. I represent the plaintiff herein, and I am fully

familiar with the above-entitled action and the facts herein recited.

3. On November 20, 1973 I received a letter from the office of the United States Attorney stating that the instant action had been dismissed for my failure to appear at a pre-trial conference held before JUDGE SYLVESTER J. RYAN on November 19, 1973. (See Exhibit "A" attached hereto and made a part hereof).

4. At no time have I ever received from anyone written or oral notice of a pre-trial conference or any other hearing of the instant action before the Court. I first learned of said pre-trial conference in said letter from the office of the United States Attorney [Exhibit "A"]. Subsequently, I have repeatedly attempted to phone the chambers of Judge Ryan to discuss the matter.

5. The dismissal of the instant action for my failure to appear at a pre-trial conference of which I had no notice works great prejudice to the plaintiff. Said dismissal constitutes a surprising and unconscionable denial of due process of law to the plaintiff. Further, said dismissal works a gross unfairness to me as attorney for plaintiff in the instant action.

WHEREFORE, affirmant respectfully prays that an order pursuant to Rule 60 of the Federal Rules of Civil Procedure, 28 U. S. C. be entered setting aside the aforesaid order of dismissal and thereby reinstating the instant action, and further

prays that a pre-trial conference be noticed by the Court pursuant to Rule 16 of the Federal Rules of Civil Procedure, 28 U. S. C.

If this relief is granted, there is no possible prejudice that would result to the defendants.

No previous application has been made for this or similar relief.

Dated: New York, New York
November 26, 1973

CARL O. CALLENDER

ORDER OF RYAN,J., RESTORING ACTION TO CIVIL DOCKET, STRIKING COMPLAINT, WITH LEAVE TO AMEND, DECEMBER 6, 1973

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY,

Plaintiff,

-v-

DR. MARTIN, et al., and THE UNITED STATES GOVERNMENT, Washington, D.C.,

Defendants.

ORDER

71 Civ. 2306 S.J.R.

At a hearing held this day, Carl O. Callender, Esq., a member of the Bar of this Court, with offices at 176 East 106 Street, New York, New York, 10029, telephone number 369-2007, appeared on behalf of the plaintiff, Otis Clay, and in support of the within motion; and Howard S. Sussman, Esq., Assistant United States Attorney, appeared in opposition thereto.

It appeared at said hearing that plaintiff Otis Clay is presently a resident of 2075 2nd Avenue, New York, New York 10029.

IT IS ORDERED:

1. That Carl O. Callender, Esq. file a notice of appearance for plaintiff herein within five (5) days from date hereof and serve a copy of said notice on the United States Attorney.

2. That the order of dismissal entered herein on November 20, 1973 be and the same is hereby vacated and this action is restored to the civil docket of this Court.

3. That the Complaint as filed herein is stricken with leave to the plaintiff to file, within twenty-five (25) days from date hereof, an amended complaint containing a short, concise statement of plaintiff's claim.

4. That the defendants file an answer to said amended complaint or otherwise move with reference thereto within twenty (20) days after it is served.

5. That after the foregoing provisions of this Order have been complied with either of the parties may apply for an order regulating discovery and pretrial proceedings.

6. In the event that the directions of paragraphs 1, 2 and 3 are not complied with, an order of dismissal may be submitted on five (5) days notice of settlement.

SO ORDERED:

December 6, 1973

s/ Sylvester J. Ryan
U. S. D. J.

I consent to the entry of the foregoing Order.

Attorney for Plaintiff

Attorney for Defendant

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Hand'd by mail
17 Dec. 73
HRC

NOTICE OF APPEARANCE

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

- X

OTIS CLAY, :

Plaintiff, : Civil Action No. 2306/71

-against- :

DOCTOR WILLIAM R. MARTIN, :
DOCTOR PETER A. MANSKY, and :
DOCTOR DONALD R. JASINSKI of :
United States Penitentiary, :
Lexington, Kentucky : NOTICE OF

-and- : APPEARANCE

THE UNITED STATES SURGEON GENERAL, :
THE UNITED STATES ATTORNEY GENERAL, :
THE DIRECTOR OF THE BUREAU OF PRISONS, :
and the UNITED STATES GOVERNMENT, :
all of Washington, D. C., :

Defendants. :

- X

S I R S:

PLEASE TAKE NOTICE, that plaintiff hereby appears in this action, and that the undersigned has been retained as attorney for said plaintiff and demands that a copy of alll

papers in this action be served on the undersigned at the address stated below.

Dated: New York, New York
December 10, 1973

Yours, etc.

CARL O. CALLENDER
Attorney for Plaintiff

Office & Post Office Address
Community Law Offices
176 East 106th Street
New York, New York 10029

TO: PAUL J. CURRAN
United States Attorney

ATTENTION: HOWARD S. SUSSMAN
Assistant United States Attorney
Attorney for Defendants

Office & Post Office Address
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

JUDGE SYLVESTER J. RYAN
CLERK OF THE COURT
United States District Court
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

COMPLAINT (FIRST AMENDED COMPLAINT)

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

----------X

O. [illegible],

Plaintiff,

-against-

Civil Action No.
2306/71

DOCTOR [illegible] R. MARTIN,
DOCTOR PETER [illegible], MANSKY, and
DOCTOR [illegible] JASINSKI all
of Lexington, Kentucky

COMPLAINT

and

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF PRISONS,
and the UNITED STATES all of Washington,
D. C.

Defendants.

----------X

THE PLAINTIFF BY CARL O. CALLENDER, ESQ., his attorney, complaining of the defendants, alleges:

1. The action arises under U.S.C., Title 28, Section 1346 (b) as hereinafter more fully appears. Additionally, plaintiff is a citizen of the State of New York and defendants are citizens of the State of Kentucky and Washington, D.C. The matter in controversy exceeds, exclusive of interest and costs, the sum of ten thousand dollars.

2. Plaintiff was a federal prisioner confined at the United States Penitentiary, Lexington, Kentucky from in or about July, 1968 to in or about September, 1970.

3. In or about May, 1970, plaintiff participated in a medical experiment conducted at the United States Penitentiary, Lexington, Kentucky. Said experiment was conducted by defendants MARTIN, MANSKY and JASINSKI, under the authority of the defendants SURGEON GENERAL, ATTORNEY GENERAL, DIRECTOR OF THE BUREAU OF PRISONS and the UNITED STATES. The experiment involved the injection of the drug Naltrexone (EN-1693A) for

the purpose of investigating the effect of said drug as a narcotic antagonist in man.

4. In or about May, 1970, plaintiff, a black male then about 51 years of age, received two injections of the drug Naltrexone (EN-1693A) from the defendants and thereafter suffered a heart attack Prior to said injections, plaintiff was informed bythe defendants that administrations of the drug Naltrexone (EN-1693A) had caused heart conditions in previous experiments with animals, but that the particular administrations to the plaintiff were safe.

5. The defendants negligently and recklessly administered the dangerous drug to the plaintiff and thereby caused the aforesaid heart attack. Further, the defendants obtained the consent of the plaintiff for said administration through misrepresentation of the dangerous quality of the drug Naltrexone (EN-1693A). As a result thereof plaintiff suffered permanent physical disabilities, suffered, and will continue to suffer great pain of body and mind, and has had his earning capacity greatly and permanently impaired.

WHEREFORE, plaintiff demands judgment against the defendants in the sum of two million dollars and costs.

Dated: New York, New York
December 31, 1973

CARL O. CALLENDER, ESQ.
Attorney for Plaintiff
Office & P.O. Address
Community Law Offices
176 East 106th Street
New York, New York 10029

71-1654
HE Submission

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

A 71

----------X

OTIS CLAY,

Plaintiff,

-against-

Civil Action No.
2306/71

DOCTOR WILLIAM F. MARTIN,
DOCTOR PETER A. MANSKY, and
DOCTOR DONALD R. JASKINSKI all
of Lexington, Kentucky

and

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL
THE DIRECTOR OF THE BUREAU OF PRISONS,
and the UNITED STATES all of Washington,
D. C.

Defendants.

----------X

AMENDED COMPLAINT

THE PLAINTIFF BY CARL O. CALLENDER, ESQ., his attorney, complaining of the defendants, alleges:

1. The action arises under U.S.C., Title 28, Section 1346 (b) as hereinafter more fully appears. Additionally, plaintiff is a citizen of the State of New York and defendants are citizens of the State of Kentucky and Washington, D.C. The matter in controversy exceeds, exclusive of interest and costs, the sum of ten thousand dollars.

2. Plaintiff was a federal prisioner confined at the United States Penitentiary, Lexington, Kentucky from in or about July, 1968 to in or about September, 1970.

3. In or about May, 1970 Plaintiff participated in a medical experiment conducted at the United States Penitentiary, Lexington, Kentucky. Said experiment was conducted by defendants MARTIN, MANSKY and JASINSKI, under the authority of the defendants

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SURGEON GENERAL, ATTORNEY GENERAL, DIRECTOR OF THE BUREAU OF PRISIONS and the UNITED STATES. The experiment involved the injection of the drug Naltrexon (EN-1693A) for purpose of investigating the effect of said drug as a narcotic antagonist in man.

4. In or about May, 1970, plaintiff, a black male then about 31 years of age, received two injections of the drug Naltrexone (EN-1693A) from the defendants and thereafter suffered a heart attack. Prior to said injections, plaintiff was informed by the defendants that administrations of the drug Naltrexone (EN-1693A) had caused heart conditions in previous experiments with animals, but that the particular administrations to the plaintiff were safe.

5. The defendants negligently and recklessly administered the dangerous drug to the plaintiff and thereby caused the aforesaid heart attack. Further, the defendants obtained the consent of the plaintiff for said administration through misrepresentation of the dangerous quality of the drug Naltrexone (EN-1693A). As a result thereof plaintiff suffered permanent physical disabilities, suffered, and will continue to suffer, great pain of body and mind, and has had his earning capacity greatly and permanently impaired.

WHEREFORE, plaintiff demands judgment against the defendants in the sum of two million dollars and costs.

Dated: New York, New York
January 3, 1974

CARL O. CALLENDER, ESQ.
Attorney for Plaintiff
Office & P. O. Address
Community Law Offices
176 East 106th Street
New York, New York 10029

ANSWER TO AMENDED COMPLAINT

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

A 73

- - - - - - - - - - - - - - - - - - -x

OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN, DOCTOR PETER A. MANSKY, and DOCTOR DONALD R. JASKINSKI, all of Lexington, Kentucky,

and

THE UNITED STATES SURGEON GENERAL, THE UNITED STATES ATTORNEY GENERAL, THE DIRECTOR OF THE BUREAU OF PRISONS, and the UNITED STATES, all of Washington, D. C.,

Defendants.

- - - - - - - - - - - - - - - - - - -x

U.S. DISTRICT COURT
FILED 1-23-74
S.D. OF N.Y.

ANSWER TO AMENDED COMPLAINT

71 Civ. 2306 (SJR)

Defendants, by their attorney, Paul J. Curran, United States Attorney for the Southern District of New York, for their answer to the Amended Complaint in this action:

1. Deny each and every allegation contained in paragraph 1 of the Amended Complaint, except admit that this purports to be an action under the Federal Tort Claims Act, 28 U.S.C. §§1346(b), 2671-2680, inclusive, that Dr. William R. Martin and Dr. Donald R. Jasinski (sued herein as "Doctor Donald R. Jaskinski") are citizens of the State of Kentucky, that Dr. Peter A. Mansky is a citizen of the State of Massachusetts, the present Acting Surgeon General is Dr. S. Paul Ehrlich whose office is located in Rockville, Maryland, the present Attorney General is William B. Saxbe whose office is in Washington, D. C., that at all relevant times the Director of the Bureau of Prisons was Norman A. Carlson, whose office is in Washington, D. C., that the United States is a corporation sovereign with its seat of

government in Washington, D. C., and state that they are without knowledge or information sufficient to form a belief as to the truth of the allegation that plaintiff is a citizen of the State of New York.

2. Deny each and every allegation contained in paragraph 2 of the Amended Complaint, except admit that on April 19, 1967, plaintiff was duly sentenced to ten years imprisonment for violation of the federal narcotics laws and thereafter committed to the custody of the Attorney General, and that, in July 1968, during the course of said custody, plaintiff was transferred to the Addiction Research Center, a laboratory of the National Institute of Mental Health, in Lexington, Kentucky, and that plaintiff remained at said Center through late 1970.

3. Deny each and every allegation contained in paragraph 3 of the Amended Complaint, except admit that on May 27, 1970, plaintiff consented to participate in a study at said Addiction Research Center of an experimental drug called Naltrexone or EN-1639A (a copy of the consent plaintiff signed is annexed hereto and marked Exhibit A), that thereafter plaintiff participated in said study, that defendants Martin, Mansky and Jasinski supervised said study, that said study was duly conducted pursuant to statutory authority and involved the injection of EN-1639A into plaintiff and other participants for the purpose of studying the effect of said drug as a narcotic antagonist in man.

4. Deny each and every allegation contained in paragraphs 4 and 5 of the Amended Complaint, except admit that plaintiff is a black male, born in 1917, that on May 28, 1970 plaintiff was administered .01 mg. of EN-1639A subcutaneously, that on June 3, 1970 plaintiff was administered .2 mg. of EN-1639A subcutaneously, and that on June 8, 1970, plaintiff sustained a myocardial infarction.

FIRST AFFIRMATIVE DEFENSE
ON BEHALF OF ALL DEFENDANTS

5. The Amended Complaint fails to state a claim upon which relief may be granted.

SECOND AFFIRMATIVE DEFENSE
ON BEHALF OF ALL DEFENDANTS

6. Plaintiff assumed the risk of the results that might follow from the administration of the drug, EM-1639A, when he consented to its administration and such consent and assumption of risk bars all recovery in this action.

THIRD AFFIRMATIVE DEFENSE
ON BEHALF OF ALL DEFENDANTS

7. The Amended Complaint does not allege the plaintiff's residence or any other basis for venue in the Southern District of New York.

FOURTH AFFIRMATIVE DEFENSE
ON BEHALF OF DEFENDANT
UNITED STATES

8. This Court lacks jurisdiction over the subject matter of this action under 28 U.S.C. §2680(a).

FIFTH AFFIRMATIVE DEFENSE
ON BEHALF OF DEFENDANT
UNITED STATES

9. This Court lacks jurisdiction over the subject matter of this action under 28 U.S.C. §2680(h) because this action asserts a claim alleged to arise out of misrepresentation.

SIXTH AFFIRMATIVE DEFENSE
ON BEHALF OF DEFENDANT
UNITED STATES

10. This Court lacks jurisdiction over the subject matter because the Amended Complaint fails to allege that plaintiff presented his claim in writing to the appropriate federal agency and that his claim was finally denied in writing as required by 28 U.S.C. §2675(a).

SEVENTH AFFIRMATIVE DEFENSE
ON BEHALF OF DEFENDANT
UNITED STATES

11. The Amended Complaint fails to allege that plaintiff presented his claim to the appropriate federal agency within two years after his claim accrued or that an action was begun within six months after the date of a final denial of the claim by the agency to which it was presented as required by 28 U.S.C. §2401(b).

EIGHTH AFFIRMATIVE DEFENSE
ON BEHALF OF ALL DEFENDANTS
EXCEPT THE UNITED STATES

12. Each of the defendants, except the United States, is immune from this suit because this suit challenges the conduct of such defendant as an officer or employee of the United States in the course of his official duties and within the scope of his employment as such officer or employee.

NINTH AFFIRMATIVE DEFENSE
ON BEHALF OF ALL DEFENDANTS
EXCEPT THE UNITED STATES

13. Each of the defendants, except the United States, is immune from this action because the conduct of such defendant on which this action is based is conduct of an officer or employee of the United States acting within the scope of his office or employment, and suit on the basis of such conduct lies only against the United States under the Federal Tort Claims Act.

TENTH AFFIRMATIVE DEFENSE
ON BEHALF OF DEFENDANTS
MARTIN, MANSKY, JASINSKI
AND THE SURGEON GENERAL

14. Defendants Martin, Mansky, Jasinski and the Surgeon General are immune from suit under the provisions of 42 U.S.C. §233.

WHEREFORE, defendants demand judgment dismissing this action, together with their costs and disbursements, and such other and further relief as is just.

Dated: New York, New York

January 23, 1974

PAUL J. CURRAN
United States Attorney for the
Southern District of New York
Attorney for the Defendants

By: William D. Brandt

WILLIAM S. BRANDT
Assistant United States Attorney
Office and Post Office Address:
United States Courthouse
Foley Square
New York, New York 10007
Telephone: (212) 264-6053 (4)

A 78

CONSENT TO EXPERIMENTAL PROCEDURE ON A PATIENT

Date 5/27/70

I authorize the NIMH Addiction Research Center of the National Institute of Mental Health to perform experimental procedures on and to administer drugs to C/Ray # 78275 (name of patient).

The nature and purpose of both the experimental procedures and the drugs to be administered, as well as the risks involved and the possibilities of complications, have been explained to me by Dr. [redacted] Donald R. Jasinski as summarized and stated below:

The experimental drug which you will receive has not been tested in man before; however, it has been extensively studied in animals and is remarkably safe. The only serious effect to health that has been observed is that in very high doses it produces nervousness, and in much higher doses, convulsions. The dose levels that these effects have been observed in animals are over 100 times the maximum dose you will receive. The purpose of this study will be to determine if this drug produces any changes in the way you feel and produces any effects that resemble those of morphine.

You will participate in these studies at weekly intervals, and when you participate the following observations will be made upon you: 1) Measurement of pupillary diameter, 2) blood pressure, 3) pulse rate, and 4) respiratory rate. In addition, you will be required to fill out the two single dose questionnaires conscientiously.

You will be awarded one day of meritorious good time and $3 of meritorious compensation for each day of participation.

Study # 144

I further fully understand that the drug treatment to be performed is experimental and unproven by medical experience and that there may be unpredictable consequences.

Signed: Otis Clay

Register No. M- [redacted] NCX

Witness: P. McCarthy

(Name and title)

Physician: Donald R. Jasinski

(Name and title)

EXHIBIT A

NOTICE OF DEMAND FOR JURY TRIAL

A 79

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN,
DOCTOR PETER A. MANSKY, and
DOCTOR DONALD R. JASINSKY,
all of Lexington, Kentucky,

-and-

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF PRISONS,
and the UNITED STATES,
all of Washington, D. C.,

Defendants.

Civil Action
No. 2306/71

NOTICE OF DEMAND FOR JURY TRIAL

SIRS:

PLEASE TAKE NOTICE that a trial by jury is hereby demanded.

Dated: New York, New York
January 21, 1974

Yours, etc

CARL O. CALLENDER, ESQ.
Attorney for Plaintiff

Office & Post Office Address
Community Law Offices
176 East 106th Street
New York, New York 10029

TO: PAUL J. CURRAN
United States Attorney
ATTENTION: WILLIAM BRANDT
Assistant United States Attorney
Attorney for Defendants

Office & Post Office Address
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

JUDGE SYLVESTER J. RYAN and
THE CLERK OF THE COURT
United States District Court
Southern District of New York
United States Court House
Foley Square
New York, New York 10007

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

A 81

[illegible],

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN,
DOCTOR PETER A. MINSKY, and
DOCTOR DONALD R. JASINSKI all
of Lexington, Kentucky

and

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF PRISONS,
and the UNITED STATES all of Washington,
D.C.

NOTICE OF MOTION
FOR LEAVE TO FILE
AN AMENDED COMPLAINT

Civil Action No.
2306/71

SIRS:

PLEASE TAKE NOTICE, that upon the affirmation of CARL O. CALLENDER, Esq., dated the 6th day of February, 1974, and the affidavit of ARTHUR C. HELTON dated the 6th day of February, 1974, and upon all proceedings had herein, the undersigned will move this Court before JUDGE SYLVESTER J. RYAN, United States Courthouse, Foley Square, New York, New York, on the 12th day of February, 1974, at 9:30 o'clock in the forenoon of that day or as soon thereafter as counsel can be heard for leave to file an amended complaint pursuant to Rule 15 of the Federal Rules of Civil Procedure, and Section 1653 of Title 28, U.S.C. on the grounds that justice so requires in order that all issues between the parties may be fully litigated in this action, as more fully appears from the affirmation of CARL O. CALLENDER, Esq. the affidavit of ARTHUR C. HELTON, and

the proposed amended complaint annexed hereto as Exhibit A, and for such other and further relief as to the Court may seem just proper.

PLEASE TAKE FURTHER NOTICE that answering affidavits, if any, shall be served upon the undersigned not later than one day before the hearing pursuant to Rule 6 of the Federal Rules of Civil Procedure of Title 28, U.S.C.

Dated: New York, New York
February 6th, 1974

CARL O. CALLENDER, Esq.
Attorney for Plaintiff
Office and P.O. Address
Community Law Offices
176 East 106th Street
New York, New York 10029

TO: PAUL J. CURRAN
Attorney for Defendants
United States Attorney for
the Southern District of New York
Attn: William S. Brandt
Assistant United States Attorney
Office and P.O. Address
United States Courthouse
Foley Square
New York, New York 10007

JUDGE SYLVESTER J. RYAN and the
Clerk of the Court
United States District Court
Southern District of New York
United States Courthouse
Foley Square
New York, New York 10007

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

A 83

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OTIS CRAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN, DOCTOR PETER A. MANSKY, and DOCTOR DONALD R. JASINSKI all of Lexington, Kentucky

and

THE UNITED STATES SURGEON GENERAL, THE UNITED STATES ATTORNEY GENERAL, THE DIRECTOR OF THE BUREAU OF PRISONS, and the UNITED STATES all of Washington, D. C.

AFFIRMATION IN SUPPORT OF MOTION FOR LEAVE TO FILE AN AMENDED COMPLAINT

Civil Action No. 2306 /71

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STATE OF NEW YORK)
: SS.:
COUNTY OF NEW YORK)

CARL O. CALLENDER, ESQ., an attorney duly admitted to practice before the Courts of the State of New York, hereby affirms under penalty of perjury as follows:

1. I am the Director of the Community Law Offices, 176 East 106th Street, New York, New York.

2. I represent the plaintiff herein, and I am fully familiar with the above-entitled action and the facts herein recited.

3. The plaintiff filed a complaint dated January 3, 1974, and the defendant filed an answer dated January 23, 1974, pursuant to the order of the court dated December 6, 1973.

4. This affirmation is submitted in support of the plaintiff's application for leave to file an amended complaint pursuant to Rule 15 of the Federal Rules of Civil

Procedure and Section 1653 of Title 28, U.S.C. The proposed amended complaint is annexed hereto as Exhibit "A"

5. The proposed amended complaint alleges fact not set forth in the complaint filed by the plaintiff and dated January 3, 1974 in the following particulars:

(a) Specification of the names of the defendants EHRLICH, SAXBE, and CARLSON in the caption and paragraph "4" of the proposed amended complaint.

(b) Substitution of the allegations of state citizenship as to defendants MANSKY and EHRLICH in the caption and paragraph "1" of the proposed amended complaint.

(c) Addition of paragraph "2" in the proposed amended complaint alleging the plaintiff's residence as the basis for venue in the Southern District of New York.

(d) Insertion of "Addiction Research Center of the National Institure of Mental Health" and "Addiction Research Center" in paragraphs "3" and "4" respectively of the proposed amended complaint in lieu of "United States Penitentiary" in paragraphs "2" and "3" respectively of the complaint filed by the plaintiff and dated January 3, 1974.

(e) Specification of the events surrounding the administrations of the drug Naltrexone (EN-1693A) to the plaintiff as set forth in paragraph "5" of the proposed amended complaint.

(f) Addition of paragraph "7" in the proposed amended complaint alleging compliance with Sections 2675(a) and 2401(b) of Title 28, U.S.C.

6. The grounds for this motion are as follows:

(a) The proposed amendments set forth above in paragraph "5", subparagraphs (a) and (b) merely name the current Surgeon General, Attorney General, and Director of the Bureau of Prisons and show the appropriate state citizenships of the defendants.

Said amendments cannot unduely prejudice the defendants because each of the defendants had been previously apprised of the pendency of the action.

(b) The proposed amendment set forth above in paragraph "5" subparagraph (c) merely shows the basis for venue in this action as appeared in the order of the court dated December 6, 1973.

(c) The proposed amendments set forth above in paragraph "5" subparagraphs (d) and (e) merely show the appropriate title of the institutional facility within which the plaintiff was confined, and the details of the administration of the drug Naltrexone (EN-1693A) to the plaintiff. Said amendments cannot unduely prejudice the defendants because said facts were previously within the knowledge of the defendants.

(d) The proposed amendment set forth above in paragraph "5" subparagraph (f) shows one of the jurisdictional bases of the action.

This is a timely, goodfaith application by the plaintiff for leave to file an amended complaint in greater particularity for the convenience of the court and the parties to the action. Further, the proposed amended complaint shows one of the jurisdictional bases of the action not alleged in the complaint filed by the plaintiff and dated January 3, 1974 as appears from subparagraph (d) above.

7. The amendments to the plaintiff's complaint cannot cause any prejudice to the defendants in maintaining their defense on the merits of the case. Denial of leave for the plaintiff to file an amended complaint will cause undue prejudice to the plaintiff's cause.

8. The attorney for the defendants refused to consent to the filing of an amended complaint without justified reason as appears from the affidavit of ARTHUR C. HELTON annexed hereto.

9. No previous application has been made by the plaintiff for this or similar relief.

Dated: New York, New York
February 6 , 1974.

Carl O. Callender

CARL O. CALLENDER

A 87

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN,
DOCTOR PETER A. MANSKY, and
DOCTOR DONALD R. JASINSKI all
of Lexington, Kentucky

and

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF PRISONS,
and the UNITED STATES all of Washington,
D.C.

AFFIDAVIT IN SUPPORT OF MOTION FOR LEAVE TO FILE AN AMENDED COMPLAINT

Civil Action No.
2306 /71

----------X

STATE OF NEW YORK)
: SS.:
COUNTY OF NEW YORK)

ARTHUR C. HELTON, being duly sworn, deposes and says:

1. I am a law student employed by the Community Law Offices, 176 East 106th Street, New York, New York, 10029.

2. On Friday, February 1, 1974, I was instructed by CARL O. CALLENDER, ESQ. to call the attorney for the defendants herein to ascertain whether the defendants would consent to the filing of an amended complaint by the plaintiff.

3. On Friday, February 1, 1974 I made said call. The attorney for the defendants stated that he was not inclined to consent to the filing of an amended complaint unless the plaintiff agreed to drop all of the defendants from the action except the UNITED STATES.

ARTHUR C. HELTON

Sworn and subscribed to
before me this 6th day of 1974

Notary Public

CORA W. THOMAS
Notary Public, State of New York
No. [illegible]
Qualified in New York County
Commission Expires March 30, 1974

EXHIBIT "A" - AMENDED COMPLAINT (PROPOSED THIRD AMENDED COMPLAINT)

A 88

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

- X

OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN,
DOCTOR DONALD R. JASINSKI,
both of the State of Kentucky,

-and-

DOCTOR PETER A. MANSKY
of the State of Massachusetts,

-and-

DOCTOR S. PAUL EHRLICH, Acting Surgeon General,
of the State of Maryland,

-and-

WILLIAM B. SAXBE, Attorney General,
NORMAN A. CARLSON, Director of the Bureau of
Prisons, and the
UNITED STATES,
all of Washington, D. C.

Defendants.

- X

Civil Action Number 2306/71

AMENDED COMPLAINT

THE PLAINTIFF by CARL O. CALLENDER, ESQ., his attorney, complaining of the defendants, alleges:

1. The action arises under U.S.C., Title 28, Section 1346(b) as hereinafter more fully appears. Additionally, plaintiff is a citizen of the State of New York and defendants

are citizens of the States of Kentucky, Massachusetts, Maryland and Washington, D.C. The matter in controversy exceeds, exclusive of interest and costs, the sum of ten thousand dollars.

2. Plaintiff resides at 2075 Second Avenue, New York, New York.

3. Plaintiff was a federal prisoner confined at the Addiction Research Center of the National Institute of Mental Health, Lexington, Kentucky, from in or about July, 1968 to in or about September, 1970.

4. In or about May, 1970, Plaintiff participated in a medical experiment conducted at the Addiction Research Center, Lexington, Kentucky. Said experiment was conducted by defendants MARTIN, MANSKY and JASINSKI, under the authority of the defendants EHRLICK, SAXBE, CARLSON and the UNITED STATES. The experiment involved the injection of the drug Naltrexone (EN-1693A) for purpose of investigating the effect of said drug as a narcotic antagonist in man.

5. On or about May 28, 1970 plaintiff, a black male then about fifty-one years of age, received an injection, upon information and belief, of one milliliter of the drug Naltrexone (EN-1693A). On or about June 3, 1970 plaintiff, upon information and belief, received an injection of two milliliters of the drug Naltrexone(EN-1693A). As a result of said injections the plaintiff, on or about June 8, 1970, sustained a heart attack. Prior to the injections, the plaintiff was informed

by the defendants that administrations of the drug Naltrexone (EN-1693A) had caused heart conditions in previous experiments with animals, but that the particular two administrations to the plaintiff were safe.

6. The defendants negligently and recklessly administered the dangerous drug to the plaintiff and thereby caused the aforesaid heart attack. Further, the defendants obtained the consent of the plaintiff for said administration through misrepresentation of the dangerous quality of the drug Naltrexone (EN-1693A). As a result thereof, plaintiff suffered permanent physical disabilities, suffered, and will continue to suffer, great pain of body and mind, and has had his earning capacity greatly and permanently impaired.

7. Upon information and belief, after sustaining said heart attack, the plaintiff presented a claim in writing to the defendants which was finally denied in writing by the defendants on or about January 13, 1971 as required by U.S.C. Title 28, Section 2675(a) and Section 2401(b). The action herein was commenced within six months after the date of the final denial of the claim by the defendants as required by U.S.C. Title 28, Section 2401(b).

WHEREFORE, plaintiff demands judgment against the defendants in the sum of two million dollars and costs.

Dated: New York, New York
February 5, 1974

CARL O. CALLENDER, ESQ.
Attorney for Plaintiff
Community Law Offices
176 East 106th Street
New York, New York 10029

NOTICE OF MOTION TO DISMISS ACTION FOR NON-COMPLIANCE WITH DECEMBER 6, 1973 ORDER

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

U.S. DISTRICT COURT
FILED 2-25-74
S.D. of NEW YORK

OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN, DOCTOR PETER A. MANSKY and DOCTOR DONALD R. JASINSKI

and

THE UNITED STATES SURGEON GENERAL, THE UNITED STATES ATTORNEY GENERAL, THE DIRECTOR OF THE BUREAU OF PRISONS and THE UNITED STATES,

Defendants.

NOTICE OF MOTION

71 Civ. 2306

(SJR)

Motion ret. March 7-1974 petitioner

S I R :

PLEASE TAKE NOTICE that, upon the annexed affidavit of William S. Brandt, and memorandum of law the undersigned will move this Court before the Honorable Sylvester J. Ryan, United States District Judge, United States Courthouse, Foley Square, New York, New York, at 10:00 a.m. on March 7, 1974, or as soon thereafter as counsel can be heard, for an order dismissing

this action for noncompliance with this Court's December 6, 1973 order, and for such other and further relief as may be just.

Dated: New York, New York

February 22, 1974.

PAUL J. CURRAN
United States Attorney for the
Southern District of New York
Attorney for Defendants.

By: _____
WILLIAM S. BRANDT
Assistant United States Attorney

Office and Post Office Address:
United States Courthouse
Foley Square
New York, New York 10007
Telephone: (212) 264-6177

TO: CARL O. CALLENDER, ESQ.
Community Law Offices
176 East 106th Street
New York, New York 10029
Attorney for Plaintiff.

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

OTIS CLAY,

Plaintiff,

- against -

DOCTOR WILLIAM R. MARTIN,
DOCTOR PETER A. MANSKY and
DOCTOR DONALD R. JASINSKI

and

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF
PRISONS,

and

THE UNITED STATES,

Defendants.

AFFIDAVIT

71 Civ. 2306 (SJR)

STATE OF NEW YORK)
COUNTY OF NEW YORK : ss.:
SOUTHERN DISTRICT OF NEW YORK)

WILLIAM S. BRANDT, being duly sworn, deposes and says:

1. I am an Assistant United States Attorney in the office of Paul J. Curran, United States Attorney for the Southern District of New York and as such, I am familiar with and in charge of this matter. I submit this affidavit in opposition to plaintiff's motion for leave to file an amended complaint and in support of defendants' motion to dismiss.

2. An account of the procedural history of this case is necessary to understand the Government's position on these motions. This action was commenced by the filing of a pro se complaint on May 24, 1971. On August 9, 1971, defendants answered the complaint. Thereafter, the case was not prosecuted until August 14, 1973, when plaintiff, through his attorney, served interrogatories. On October 26 and November 20, 1973, defendants answered the interrogatories.

3. On November 26, 1973, this action was dismissed for lack of prosecution. On December 6, 1973, the order of dismissal was vacated and the action restored to the docket on the following grounds:

> "3. That the Complaint as filed herein is stricken with leave to the plaintiff to file, within twenty-five days from the date hereof, and amended complaint containing a short, concise statement of plaintiff's claim."

This order further provided:

> "6. In the event that the directions of paragraph . . . 3 are not complied with, an order of dismissal may be submitted. . ."

4. Although the court's order was complied with in form, it was not complied with in substance. On January 2, 1974, a "complaint" was served. On January 3, 1974, an "amended complaint" was filed. (It is difficult to ascertain the distinction between the two complaints.) At that juncture three complaints had been either served or filed in this action, all of which were defective on their face. The complaints were defective on the grounds of venue, subject matter jurisdiction and improper parties as defendants.

5. Thereafter, I called Carl O. Callender, attorney for plaintiff, to discuss the defects in the complaints. Mr. Callender never returned any of my calls. Instead, I was required to speak on several occasions to Mr. Helton, a law student employed by Mr. Callender. I discussed the defects in the complaint with Mr. Helton and requested that he clarify the complaint and correct the defects. However, not being an attorney, Mr. Helton was unable to make any commitments.

6. On January 23, 1974, an answer to the complaint was filed raising ten affirmative defenses. A review of defendants' answer amply demonstrates both the inherent confusion within the complaint, the jurisdictional defects and the obvious impropriety of certain defendants as parties.

Affirmed
71-1654
D-44

7. In light of the obvious defects, I was not surprised that Mr. Helton called on Friday, February 1, 1974, to seek my consent to the filing of a third amended complaint in this action. I did tell Mr. Helton that I was inclined not to grant his request for several reasons including the fact that I was of the opinion that his proposed amendments would not cure the glaring defects in his complaint, i.e., improper parties. I told Mr. Helton that if he would agree to bring suit against the United States alone, he would then have a proper party defendant under the Federal Tort Claims Act and a defendant who was in a position to pay the alleged $2,000,000 in damages. However, I told Mr. Helton that I would like to think about this matter until February 6, 1974. Due to the press of other matters I was unable to call Mr. Helton on February 6, 1974. Rather than extending the courtesy of calling me on February 6, to ascertain my response, Mr. Helton prepared an affidavit on that date and on February 7, filed the motion papers. I relate these facts not to create an air of acrimony but rather to demonstrate that this office has sought to cooperate with plaintiff throughout the two and one half years that this matter has been pending.

8. Although in good faith the defendants cannot claim that they will be unduly prejudiced by defendants filing a fourth complaint in this action they do wish the court to consider the following. It is respectfully submitted that plaintiff is and will be in violation of this court's December 6, 1973 order, requiring the complaint to concisely state plaintiff's claim. Presently, the complaint is a poorly pleaded mixture of claims against individuals, doctors, representatives of government agencies and the United States. There are insufficient factual allegations to state a claim for relief against the individual Government defendants.

Moreover, 42 U.S.C. § 233 clearly bars the suit against the individual doctors and the Surgeon General. It is respectfully submitted that this Court's December 6, 1973 order should be viewed as an order pursuant to Rule 12(e) of the Federal Rules of Civil Procedure which was not complied with. Therefore, if defendant's are required to answer they will once again have to respond to a vague and ambiguous complaint. In any case, the plaintiff's have failed to comply with this court's previous directives. For these reasons the complaint should be dismissed.

9. Defendants submit that it is manifestly unfair that after they have twice answered, set forth their defenses and answered interrogatories, plaintiff should utilize those answers as a learning tool to correct the defects in the complaint. There must come a point when the pleadings must cease. Defendants respectfully submit that the time has now come. This was the purpose of the Court's December 6 order. The filing of an amended complaint should not be allowed and in fact, the complaint should be dismissed.

10. However, if the court deems it appropriate to grant plaintiff's motion and deny defendants' motion, the defendants' respectfully request 25 days to answer or to otherwise move against the complaint. In the alternative, defendants' request that plaintiff's motion to amend be granted on terms, i.e., that the action be brought only against the United States, who is clearly the proper defendant.

WHEREFORE, it is requested that plaintiff's motion to amend the complaint be denied and that the complaint be dismissed pursuant to the Court's December 6, 1973 order.

/s/
WILLIAM S. BRANDT
Assistant United States Attorney

Sworn to before me this
22 day of February, 1974.

[illegible] Clerk
[illegible] County
[illegible] 30, 1975

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

- X

OTIS CLAY,

Plaintiff,

-against-

DOCTOR WILLIAM R. MARTIN,
DOCTOR PETER A. MANSKY, and
DOCTOR DONALD R. JASINSKI,
all of Lexington, Kentucky,

-and-

THE UNITED STATES SURGEON GENERAL,
THE UNITED STATES ATTORNEY GENERAL,
THE DIRECTOR OF THE BUREAU OF PRISONS,
and THE UNITED STATES,
all of Washington, D. C.,

Defendants.

Civil Action
No. 2306/71
(S.J.R.)

AFFIRMATION

- X

STATE OF NEW YORK)
: ss.:
COUNTY OF NEW YORK)

CARL O. CALLENDER, ESQ., an attorney duly admitted to practice before the Courts in the State of New York, hereby affirms under penalty of perjury as follows:

1. I am the Director of Community Law Offices and I represent the plaintiff herein. I am fully familiar with the above-entitled action and the facts herein recited.

2. This affirmation is submitted in opposition to the defendants' motion in opposition to the plaintiff's application for leave to file an amended complaint in the action.

3. The defendants' motion is reprehensible submitted in opposition to the plaintiff's application for leave to file an amended complaint despite the fact that the February 18, 1974 hearing date for the plaintiff's application is long since past. (See paragraph "1" of the affidavit of WILLIAM S. BRANDT, ESQ., dated February 22, 1974 hereinafter referred to as "BRANDT Affidavit"). Further, the defendants have not moved before the Court to enlarge the period of time specified in which to oppose the plaintiff's application. The law clerk to JUDGE RYAN informed my office on February 11, 1974 that the plaintiff's motion would be deemed "submitted" due to JUDGE RYAN's regrettable illness.

4. Pursuant to the order of December 6, 1973 of JUDGE RYAN, on January 2, 1974 the plaintiff served a "complaint" dated December 31, 1973 on Mr. Howard S. Sussman, the then Assistant United States Attorney in charge of the matter. The complaint was filed and returned by the Clerk of the Court for my signature and so that it might be retitled "amended complaint". It was then dated January 3, 1974. The defendants apparently construed this clerical transaction as an amendment as a matter of course despite the fact that in all other respects the "complaints" are identical. (See

paragraph "4" of BRANDT affidavit). This construction may be explained by the fact that, as far as I know, Mr. BRANDT was not yet the Assistant United States Attorney in charge of the matter at the time of the transaction.

5. The defendants also seek to characterize the order of the Court of December 6, 1973 vacating an order of dismissal pursuant to Rule 60 of the Federal Rules of Civil Procedure, 28 U. S. C., as an order made pursuant to Rule 12(e) of the Federal Rules of Civil Procedure, 28 U. S. C. (See inter alia paragraphs "1" and "8" of BRANDT affidavit). The order of December 6, 1973 was made in response to the plaintiff's motion to vacate an order of dismissal entered at a pre-trial conference in the matter of which the plaintiff and his attorney were never notified. The order did not point out any defects or any details to be specified beyond "a short concise statement of plaintiff's claim". A reading of the complaint filed by the plaintiff and dated January 3, 1974 shows compliance in substance with the order of the Court and the pleading requirements of Rule 8(a) of the Federal Rules of Civil Procedure, 28 U. S. C.

6. Further, the defendants cannot possibly claim that they meet the test under Rule 12(e) of the Federal Rules of Civil Procedure, 28 U. S. C. that they cannot reasonably be required to frame a responsive pleading. On January 23, 1974 the defendants answered with particularity the complaint filed by the plaintiff on January 3, 1974. The defendants

have not moved before the Court for further statements.

7. The plaintiff seeks leave to file an amended complaint in greater particularity for the convenience of the Court and the parties to the action. Further, the proposed amendments show one of the jurisdictional bases of the action not alleged in the complaint filed by the plaintiff and dated January 3, 1974. The defendants admit that the amendments to the plaintiff's complaint cannot cause any prejudice to the defendants. (See paragraph "8" of BRANDT affidavit). The attorney for the defendants surely cannot characterize as "unfair" the work involved in answering the proposed amended complaint when said answer would likely involve simply deleting the third, sixth, and seventh affirmative defenses set out in the defendants' answer of January 23, 1974. (See paragraph "9" of BRANDT affidavit).

8. The defendants seem to rely in passing on Section 233 of Title 42 U. S. C. (See paragraph "8" of BRANDT affidavit). Whether the defendants are officers or employees and are acting within the scope of their office or employment for the purposes of the remedy provided by Section 1346(b) of Title 28 U. S. C. and all related provisions, including Section 233 of Title 42 U. S. C. is a question of fact in the instant case to be resolved at trial. If under the circumstances of the instant case it appears that the defendants are not officers or employees acting within the scope of their office or employment for the purposes of the remedy provided by

Section 1346(b) of Title 28 U. S. C. and all related provisions, when the plaintiff has available the additional basis of diversity jurisdiction which is alleged in the amended complaint upon which to seek relief.

9. The plaintiff submits that the defendants' motion cannot show a basis either to deny plaintiff's application for leave to file an amended complaint or to dismiss the action. Thus, the effect of the defendants' motion is at best dilatory.

WHEREFORE, it is requested that plaintiff's application for leave to file an amended complaint be granted.

Dated: New York, New York
March 4, 1974

CARL O. CALLENDER, ESQ.
Attorney for Plaintiff

Office & Post Office Address
Community Law Offices
176 East 106th Street
New York, New York 10029

TO: PAUL J. CURRAN
Attorney for Defendants
United States Attorney for the Southern District of New York
ATTENTION: William S. Brandt
Assistant United States Attorney
United States Courthouse
Foley Square
New York, New York 10007

JUDGE SYLVESTER J. RYAN and the
CLERK OF THE COURT
United States District Court
Southern District of New York
United States Courthouse
Foley Square
New York, New York 10007

ENDORSEMENT AND ORDER OF RYAN, Jr., DENYING MOTION TO SERVE AN AMENDED COMPLAINT AND GRANTING DEFENDANTS' MOTION TO DISMISS

A 102

U.S. DISTRICT COURT
FILED
MAR 14 1974
S.D. OF N.Y.

OTIS CLAY v. DOCTOR WILIAM R. MARTIN et al.

Endorsement
71 Civ. 2306

This action was commenced by the filing of a Pro Se complaint on May 24, 1971; defendants answered this complaint on August 9, 1971. Thereafter, plaintiff did nothing to prosecute the action until August 14, 1973 when, through his attorney, he served interrogatories, which defendants thereafter answered.

This action was dismissed for lack of prosecution on November 26, 1973. The order of dismissal was later vacated "with leave to the plaintiff to file, within twenty-five days....an amended complaint containing a short, concise statement of plaintiff's claim." Although plaintiff filed what he calls an amended complaint on January 4, 1974, it differs in no respect with the prior complaints of plaintiff. All of plaintiff's complaints are defective as to venue, subject matter, jurisdiction and improper parties as defendants. These objections were set forth and pleaded in the ten affirmative defenses which were filed as an answer to plaintiff's new complaint herein on January 23, 1974.

The plaintiff again moves for leave to file a further amended complaint, and this motion is opposed by the United States Attorney representing the named defendants, and the United States Attorney also moves to again dismiss the action.

Upon the file and record, the plaintiff's motion to serve a further amended complaint is denied and defendants' motion to dismiss is granted. The Complaint is dismissed upon the merits and the Clerk is directed to enter such judgment promptly without further order.

So ordered.

Dated: March 14, 1974.

SYLVESTER J. RYAN
U.S.D.J.

ONLY COPY AVAILABLE